ARCHIVES OF SURGERY

VOLUME 39 JULY 1939 NUMBER 1

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LIPID AMINO NITROGEN CONTENT OF THE BLOOD IN DISEASES OF THE LIVER AND OF THE BILIARY TRACT

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Despite many experimental and clinical investigations, knowledge of the exact nature of the substances and reactions involved in the process of coagulation of the blood is still incomplete. Information concerning the defects of coagulation present in such conditions as hemophilia, jaundice and purpura is even more deficient. Until these fundamental defects are elucidated it is evident that the treatment of these conditions must remain empiric and that the prognosis for any given patient will continue to be uncertain.

Eagle [1] has recently summarized the available evidence on the clotting mechanism and supported the theory that the formation of a blood clot is the result of two basic reactions. The first is the reaction between prothrombin, calcium and a tissue or platelet derivative (thromboplastin) to form thrombin; the second, the action of thrombin on fibrinogen to form fibrin. A substance, antithrombin, normally present in the circulating blood, or heparin, prepared artificially from dog's liver, may prevent the coagulation of blood by inhibiting the formation of thrombin from its precursors.

The tendency to hemorrhage seen in some cases of obstructive jaundice is particularly serious because many of the patients require surgical procedures to avert the disastrous effects of prolonged cholemia. Hemorrhage plays a major role in the relatively high postoperative mortality of this condition and has prompted many investigations of the clotting mechanism and its defects. Abnormalities or deficiencies in practically all of the recognized factors have been sought for, with varied success.

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1. Eagle, H.: Medicine **16**:95, 1937.

In the course of investigations into the hemorrhagic tendency in jaundice, our attention was directed by some experiments performed by Hellman [2] toward a study of the possible role of alterations of the lipid amino nitrogen of the blood as a factor in this diathesis. Howell [3] ascribed the coagulating activity of lipid extracts of the tissues to the monoaminophospholipid cephalin. Recent work of certain investigators [4] casts doubt on the role of cephalin as the thromboplastic substance. Nevertheless, it is conceivable that thromboplastic activity may be due to some substance closely related to cephalin.

The development by Van Slyke and his associates [5] of new procedures for the determination of the blood lipids has made possible an approach to the problem of the relation of amino lipids to coagulation of the blood by quantitative chemical methods. The chemical method is not specific for cephalin but determines all the primary amino nitrogen in the soluble extractives of the blood that are soluble in alcohol and ether or in purified petroleum benzine (petroleum ether). In the presence of phospholipids a small amount of urea, a compound with a primary amino group which reacts with nitrous acid, is also dissolved in the extractives.

The first experiments involved determination of the lipid amino nitrogen content of the blood of dogs after experimental ligation of the common bile duct. In the first animal, after a control period of forty days, during which time the values for lipid amino nitrogen in 9 determinations ranged between 1.8 and 3 mg. per hundred grams of whole blood, the common duct was doubly ligated and divided. This procedure produced a transient rise, followed by a fall to 0.6 mg. after thirty days (chart 1).

Further experiments showed that a progressive fall in the lipid amino nitrogen content of the blood after ligation of the common bile duct was not a constant finding. In some dogs there was a conspicuous increase of the lipid amino nitrogen before death (chart 2). At autopsy the pathologic conditions observed in dogs with a progressive decrease were different from those in dogs with a terminal increase. In the former, obstructive biliary cirrhosis was the only change in the liver, while in the latter there were cholangitis and multiple abscesses of the liver. In 1 animal in which the lipid amino nitrogen decreased, death resulted from hemorrhage into the operative field after a cholecysto-

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2. Hellman, L. M.; Moore, R. A., and Andrus, W. DeW.: Proc. Soc. Exper. Biol. & Med. **36**:176, 1937.

3. Howell, W. H.: Am. J. Physiol. **29**:187, 1911.

4. Fischer, A., and Hecht, E.: Biochem. Ztschr. **269**:115, 1934. Charles, A. F.; Fisher, A. M., and Scott, D. A.: Tr. Roy. Soc. Canada (Sect. 5) **28**: 49, 1934.

5. Kirk, E.; Page, I. H., and Van Slyke, D. D.: J. Biol. Chem. **106**:203, 1934.

duodenostomy. In the other animals there was no apparent correlation between the altered values for lipid amino nitrogen and a tendency to hemorrhage in dogs with obstructive jaundice.

Although the results in animals were inconclusive, it seemed desirable to study the lipid amino nitrogen in man. Determinations on 22 patients without clinically detectable disease of the liver gave an average value

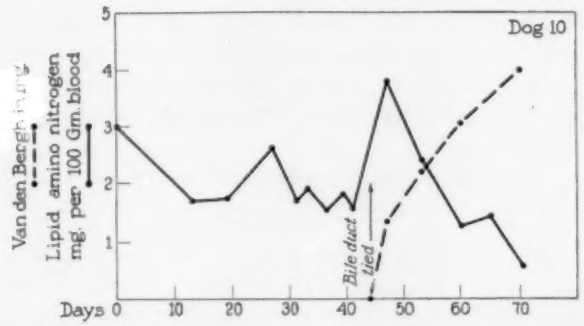

Chart 1.—Lipid amino nitrogen content of the blood after experimental ligation of the bile duct.

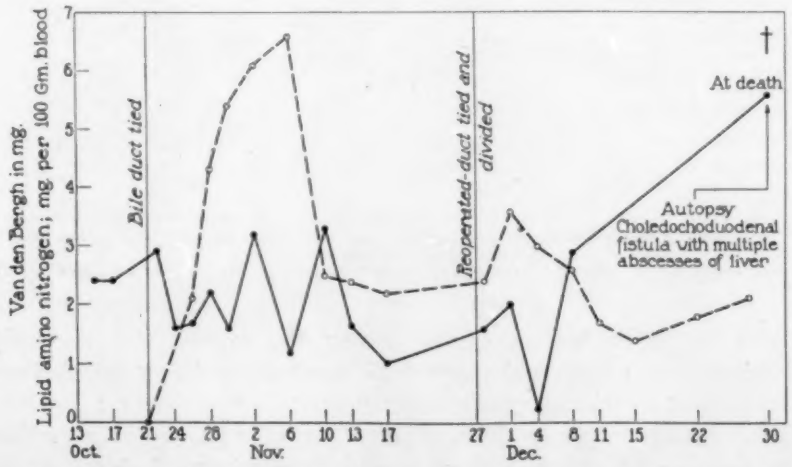
Van den Bergh in mg.
Lipid amino nitrogen; mg. per 100 Gm. blood
Bile duct tied
Reopened-duct tied and divided
At death
Autopsy
Choledochoduodenal fistula with multiple abscesses of liver
13 17 21 24 28 2 6 10 13 17 27 1 4 8 11 15 22 30
Oct. Nov. Dec.

Chart 2.—Increase of the lipid amino nitrogen content of the blood before death.

of 1.24 per hundred grams of blood, with a standard deviation of 0.62. As is shown in the table, 128 determinations on 43 patients with jaundice or with other conditions associated with hemorrhage or damage to the liver were made.

One of the first patients studied had severe obstructive jaundice associated with carcinoma of the cystic duct. Death occurred nine days

after an exploratory laparotomy, with hemorrhage into the wound and in the tissues about the carcinoma. In this patient (chart 3) the value for lipid amino nitrogen was elevated above the average normal and terminally reached the extraordinarily high level of 12 mg. per hundred grams of blood. Two additional patients with hemorrhage and terminal increase of the lipid amino nitrogen to 4 and 6 mg. respectively have been observed. The occurrence of extensive hemorrhage in these 3 patients at a time when the lipid amino nitrogen was increased throws doubt on the role of lipid amino compounds in the coagulation of blood. There are two possible explanations of the discrepancy: first, that nonlipid amino compounds, such as urea, were

Conditions in Which the Lipid Amino Nitrogen Content of the Blood Was Studied

Diagnosis	No. of Cases	No. of Determinations
Common duct stone	4	30
Catarrhal jaundice	5	14
Carcinoma of the bile ducts or pancreas	5	38
Other carcinomas	3	3
Hemolytic jaundice	2	5
Hepatic disease *	3	6
Thrombopenic purpura	2	8
Chronic cholecystitis	3	3
Hemorrhage †	6	7
Pernicious anemia	1	1
Goiter	3	3
Miscellaneous conditions (patients moribund) ‡	4	4
Diabetes	1	2
Chronic cholangitis	1	4
	43	128
Controls	22	23
	65	151

* One case each of abscess of the liver, arsphenamine poisoning and atrophy of the liver.
† Due to causes other than jaundice or thrombopenic purpura.
‡ One case each of abscess of the brain, septicemia, abscess of the lung and fracture of the skull.

included in the extractives of the blood; and second, that the lipid extractives have an optimal concentration, above or below which they are ineffectual as thromboplastic substances.[6]

Five patients (chart 4) with catarrhal jaundice showed no elevation of the lipid amino nitrogen above normal despite icteric indexes which at times reached 150. The same findings were observed in 4 patients with stone in the common bile duct. In these 9 instances of jaundice uncomplicated by severe damage to the liver the values for lipid amino nitrogen remained normal.

Two additional patients with carcinomatous obstruction of the biliary tract are of importance in bridging the gap between the findings

6. Wadsworth, A.; Maltaner, F., and Maltaner, E.: J. Immunol. **30**:417, 1936.

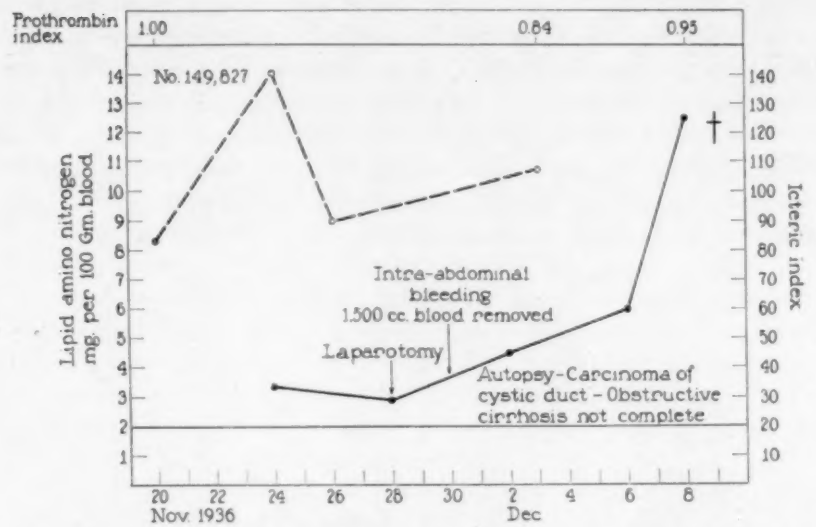

Chart 3.—Antemortem elevation of the lipid amino nitrogen content of the blood of a patient with carcinoma of the cystic duct and obstructive cirrhosis.

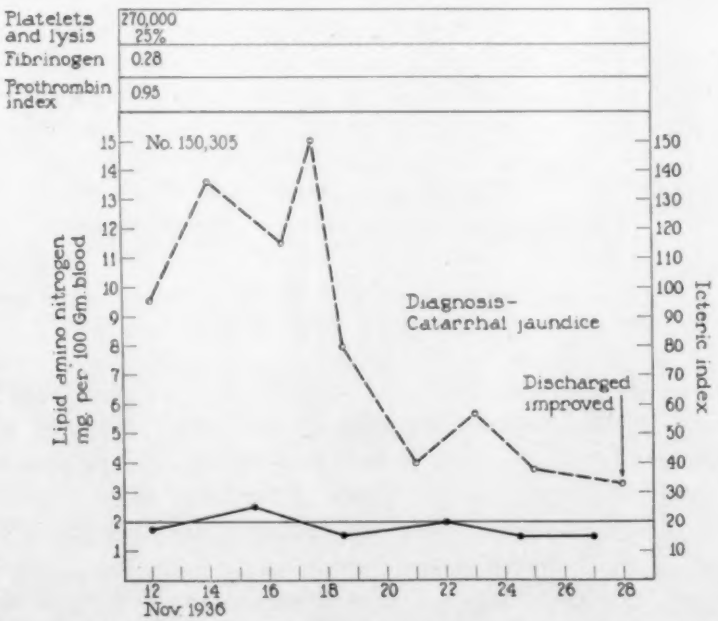

Chart 4.—Lipid amino nitrogen content of the blood in a case of catarrhal jaundice.

in patients with hemorrhage and increased values of the lipid amino nitrogen content of the blood and those with no hemorrhage and with normal values. In 1, a patient with obstructive jaundice (icteric index, 80) due to carcinoma of the head of the pancreas, who was not operated on but died of bronchopneumonia, the values for lipid amino nitrogen remained within normal limits. In the other, a patient with carcinoma of the gallbladder, metastases to the liver and obstructive cirrhosis (determined by biopsy), the value reached 6 mg. before death. Neither patient showed evidence of hemorrhage.

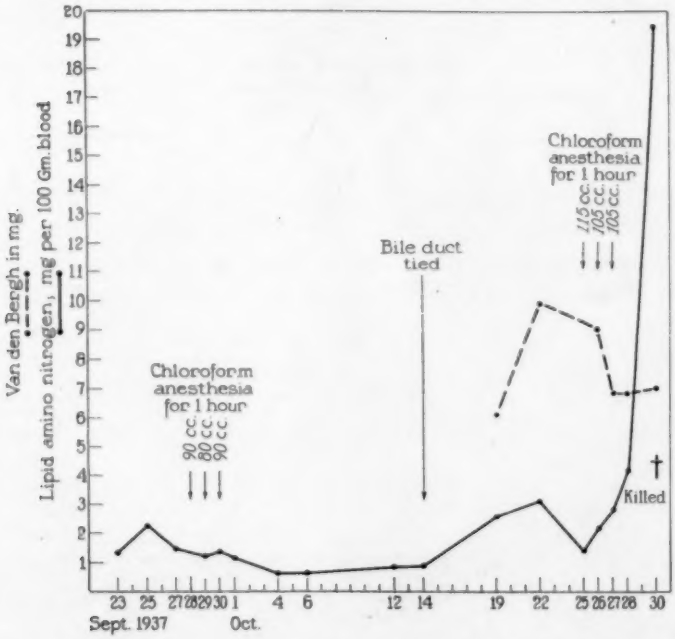

Chart 5.—Effect of chloroform anesthesia, with and without obstructive jaundice, on the lipid amino nitrogen content of the blood.

Three patients with carcinoma of organs other than the liver, pancreas or biliary ducts uniformly showed values for lipid amino nitrogen within normal limits. The same was true of 4 patients moribund from causes not related to disease of the liver.

It would seem, therefore, that the findings in man have a similarity to those in dogs. When severe damage to the liver was present, the values for lipid amino nitrogen were elevated above 2 mg. and tended to ascend still higher before death, while patients with jaundice, however severe, unassociated with demonstrable damage to the liver showed values below 2 mg. at all times.

In 2 patients with congenital hemolytic jaundice and in 2 patients with thrombopenic purpura the values for lipid amino nitrogen were normal and showed no change after splenectomy.

With this information obtained from observations in man, indicating the significance of damage to the liver as a factor in the elevation of the lipid amino nitrogen content of the blood, further experiments were carried out on animals with substances known to produce damage to the liver. These included prolonged chloroform anesthesia and the injection of phosphorated oil and of carbon tetrachloride. In animals without obstruction of the common duct no significant changes in the levels of lipid amino nitrogen resulted. On the contrary, the administration of chloroform to 3 animals with obstruction of the common bile duct was followed by a conspicuous increase of the lipid amino nitrogen in the blood (chart 5). In 1 animal with obstruction of the common bile duct the injection of phosphorated oil did not result in an increase. These observations indicate that the liver of an animal with obstructive jaundice is more sensitive to damage than that of a normal animal. The livers of the animals with obstructive jaundice and chloroform poisoning showed profound fatty degeneration and necrosis of the entire lobule, together with the usual changes of obstructive cirrhosis.

In a further attempt to shed some light on the metabolism of lipid amino nitrogen, experiments on the effect of hemorrhage and of a permanent biliary fistula were carried out. In 2 dogs, the withdrawal of sufficient blood to produce a reduction in blood volume of approximately one third in a three day period failed to cause any appreciable alteration in the level of the lipid amino nitrogen of the blood. In man, 7 determinations in 6 patients with severe hemorrhage from peptic ulcer were within the normal range. In a dog with a biliary fistula there was no significant change in the lipid amino nitrogen in a period of sixty days.

CONCLUSIONS

1. The normal lipid amino nitrogen content of the blood averages 1.24 mg. per hundred grams of whole blood, with a standard deviation of 0.62.

2. In patients with obstructive or hemolytic jaundice but without evident damage to the liver the lipid amino nitrogen content of the blood is within normal limits.

3. In patients with obstructive jaundice and damage to the liver there is consistent elevation of the lipid amino nitrogen content of the blood above 2 mg. per hundred grams of whole blood.

4. There is no apparent correlation between the hemorrhagic diathesis in obstructive jaundice and the level of lipid amino nitrogen in the blood.

LARYNGEAL SPASM AND SO-CALLED TRACHEAL COLLAPSE

EXPERIMENTAL AND CLINICAL STUDIES

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The experiments herein reported were performed in an attempt to explain serious stridor arising in a patient on whom thyroidectomy was being performed.

The patient was a middle-aged man with an average degree of hyperthyroidism of a toxic diffuse type. A routine thyroid incision, splitting the ribbon muscles in the midline, was made with the patient under ethylene anesthesia. When hemostats were put on the capsule of the right lobe preparatory to excision of the lobe, mild stridor developed. During the process of excising the lobe, mild tension was applied on it to effect delivery. The stridor increased markedly, until it became so severe as to indicate almost complete obstruction of the airway by the time the excision had approached the trachea. A rapid search was made for the recurrent laryngeal nerve; it was found lying in the usual position, but no clamps were within ¼ inch (0.6 cm.) of it at any point. Since there appeared to be no hemostats on the nerve, but more particularly since the stridor had developed before the thyroid lobe was cut, it was felt the stridor was of reflex origin and not the result of direct trauma to the nerve. The operation was stopped and all tension released for at least a minute, but the stridor persisted. The isthmus was then rapidly undercut and the trachea exposed. The trachea was no larger than a lead pencil and appeared bloodless. Again all tension was released, the weight of the clamps being taken off the neck, and two or three minutes elapsed before it was decided that a tracheotomy should be done. By this time the patient was extremely cyanotic and was getting practically no air through the larynx. However, at this point the airway began to open, and after about four or five minutes the patient was breathing in a normal fashion. The anesthetist had been giving ethylene but had changed to pure oxygen during the respiratory difficulty. It appears that the patient's relief was caused more by the release of the trachea from the isthmus, with consequent relaxation, and by stopping the operative procedure than by changes in the anesthetic procedure alone. When the trachea was observed again after the patient had recovered from the laryngeal obstruction, it had enlarged to at least the size of one's index finger and was unusually pink. This marked change in size was noted by the entire operating team and was too pronounced to be an erroneous observation. It appeared then that the trachea had actually undergone a spasm, which had produced a marked decrease in size, or that negative pressure incident to a laryngeal obstruction was instrumental in

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Presented at the Third International Goiter Conference, Washington, D. C., Sept. 12-14, 1938.

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causing a partial collapse of the tracheal walls. However, while the necessity of tracheotomy was being debated the patency of the lumen was proved by aspirating the trachea with a hypodermic needle and syringe to identify it in case tracheotomy would have to be done. The trachea was so small and covered with sufficient areolar and fibrous tissue that one could scarcely be certain of its identity. The patient recovered so well from the respiratory obstruction that the operation was continued and the left lobe resected. This was done without any evidence of respiratory obstruction. At no time in the postoperative course did the patient have any respiratory difficulties. Laryngoscopic examination of the vocal cords revealed normal action.

Numerous instances of a similar but less severe nature have been encountered by me as well as by practically all other surgeons. In my experience stridor develops most commonly while the superior thyroid artery is being isolated and ligated. I have heard of several tracheotomies being performed under similar circumstances, but with immediate recovery after operation, thus allowing the tracheotomy tube to be removed within twenty-four hours. The routine anesthetic in use during my own work has been ethylene. Occasionally ether has been given in experimental fashion during the mild episodes of stridor. The ether actually appeared to be of definite though mild assistance in eliminating stridor. Obviously the anesthetists make all attempts to eliminate anoxia during the complication. Anoxia will undoubtedly be associated with all instances of severe adductor spasm of the larynx. However, it is probable that the anoxia per se does not increase the spasm but in reality tends to relieve the condition by its reflex action toward dilation of the larynx. Anesthetists have noted at times that administration of oxygen relieves stridor. In some instances it is probable that relief is brought about not by the oxygen per se but by dilution of the anesthetic agent, which by reflex action was the primary cause of the laryngeal (or tracheal) spasm. In reviewing the cases it does not appear that the patients suffering this complication had preliminary anoxia incident to the anesthetic. Several theories may be proposed to explain stridor, namely, laryngeal spasm, tracheal spasm and tracheal collapse. It was because of the inability to explain this complication that the experiments herein described were conducted. When stridor occurs during manipulation of the superior pole, injury to the superior laryngeal nerve must be considered, as is discussed later. Without doubt, light anesthesia encourages development of stridor.

ANATOMY AND PHYSIOLOGY

Trachea.—The cartilaginous rings of the trachea, varying between fifteen and twenty in number, are horseshoe shaped and connected to each other by the fibroelastic membrane, in which the rings are embedded. The posterior fourth of the trachea is made up of the trachealis muscle, which in the human being is attached primarily to

the tips of the rings, but some fibers may be attached to the inner and outer surfaces of these rings near the tips as well as to the fibroelastic membrane between the rings. In the dogs examined by me a portion of the muscle was attached to the tips of the rings, but most of it was attached to the outer surface of the rings and the adjacent fibroelastic membrane. Contraction of the trachealis muscle will appreciably narrow the width of the tracheal lumen. The amount of constriction attainable by contraction of the trachealis muscle varies considerably, even in normal persons, because of the variation in the strength of the carti-

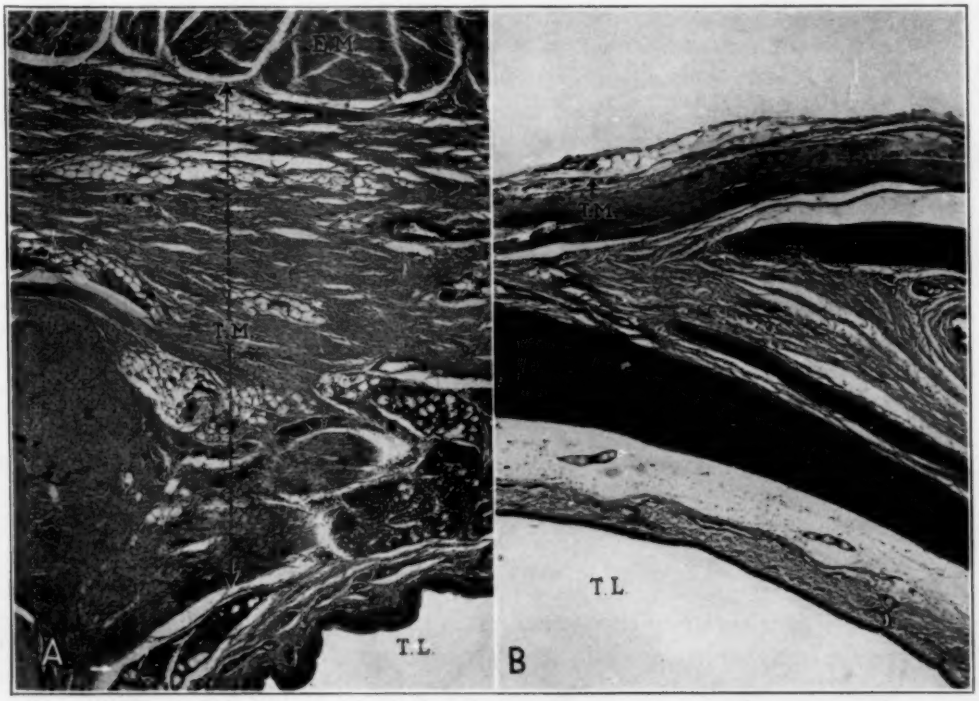

Fig. 1.—*A*, low power photomicrograph showing a section through the posterior portion of the trachea of a human being. *T. M.* indicates the tracheal muscle; *T. L.*, the tracheal lumen, and *E. M.*, the esophageal muscles. *B*, low power photomicrograph of the posterior portion of the dog's trachea. Note that the thickness of the trachealis muscle which is indicated in each photomicrograph (*T. M.*) is comparatively much greater in the human being than in the dog. Theoretically the trachealis muscle of the human being would be capable of more contraction than that of the dog, but proof of this is not at hand.

laginous rings. A decrease in the strength or support offered by these rings is noted in certain constitutional diseases, but more particularly when a thyroid nodule compresses the trachea over a long period. In the latter instance, as will be discussed later, the erosion or atrophy

of a few cartilaginous rings at the site of pressure by the adenoma may be almost complete. Experiments to be described show conclusively that stimulation of the trachealis muscle of the dog with an electric current produced a pronounced contraction. To my knowledge the results of similar experiments on the human trachea are not available, but a comparison of the amount of trachealis muscle shows a greater quantity in the human being than in the dog (fig. 1), implying that the constricting effect on the trachea could be equally, if not more, prominent in the human being than in the dog. The trachealis muscle in the human being is supplied by the recurrent laryngeal nerve and in the dog by the pararecurrent nerve (fig. 2). Although fixed posteriorly to prevent traction on

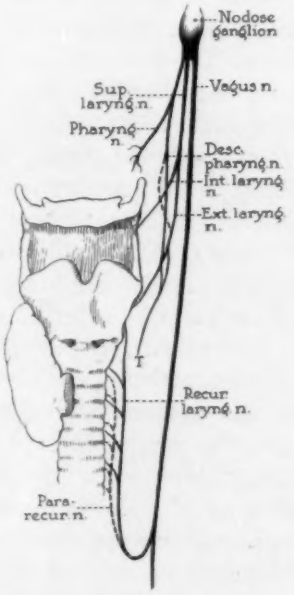

Fig. 2.—Nerve supply of the larynx. The nerves shown by the dotted lines are the pararecurrent nerve and a descending branch of the pharyngeal nerve, which represent the two main points of difference in the nerve supply of the larynx in the dog and the human being. In the dog the cricothyroid muscles are frequently innervated by a branch of the pharyngeal ramus of the vagus nerve.

the lungs by movement of the head, the trachea is elastic and thereby allows for stretching. Another important protective mechanism afforded by elasticity of the trachea lies in the fact that compression of the trachea by tumors in the neck is minimized by deviation made possible by tracheal elasticity.

The function of the trachealis muscle in primitive life was no doubt primarily related to constriction of the tracheal lumen during expiration, to eliminate as much dead space air as possible, thereby aiding in

endurance of the animal as far as activity is concerned. Negus [1] has called attention to the fact that the trachealis muscle is extremely thick in the horse and, being attached high on the cartilaginous rings, would by contraction be effective in expelling dead space air during expiration. However, this expiratory movement is not present in the human being, as determined by observation during thyroidectomy. It would appear then that as man developed past the scale where physical endurance was important in the maintenance of life, this function was being lost, although there is good evidence that the trachealis muscle is capable of contraction with consequent narrowing of the lumen of the trachea.

Larynx.—Authorities differ as to the number of intrinsic muscles in the larynx, because of the complicated way in which the various muscle bundles intermingle. The numbers given vary between eleven and nineteen. All except the interarytenoid muscles are paired. The intrinsic muscles may be classified into three groups. The constrictor group, including the adductors of the vocal cords, consist of the lateral cricothyroid, the interarytenoid, the thyroarytenoid, the oblique arytenoid and the aryepiglottic muscles. The dilator muscles of the larynx, including the abductors of the vocal cords, are the posterior cricoarytenoid and possibly the thyroepiglottic muscles. A third group is instrumental primarily in modifying tension of the vocal cords: The cricothyroid muscles produce tension on the cords, whereas the internal thyroarytenoid (vocalis) muscles produce relaxation of the cords. In number, mass and muscle power the adductors predominate over the abductors, a factor which in itself may be of importance in explaining the readiness with which adductor spasm is produced.

There is slight difference of opinion regarding the innervation of these muscles. Most textbooks on anatomy state that the cricothyroid muscles are innervated by the external branch of the superior laryngeal nerve and all the remaining intrinsic muscles by the recurrent laryngeal nerve.

There is likewise a difference of opinion regarding the position of the recurrent laryngeal nerve as related to the inferior thyroid artery. Berlin and Lahey [2] noted that in 18 of 23 cadavers the nerve on the right was anterior to the artery, whereas it was posterior to the artery on the left side in 19 of 22 instances. In 4 of the 19 instances the nerve was posterior to the lower branch but anterior to the upper branch of the

1. Negus, V. E.: The Mechanism of the Larynx, St. Louis, C. V. Mosby Company, 1930.

2. Berlin, D., and Lahey, F. H.: Dissection of Recurrent and Superior Laryngeal Nerves: Relation of Recurrent to Inferior Thyroid Artery and Relation of Superior to Abductor Paralysis, Surg., Gynec. & Obst. **49**:102, 1929.

artery. Nordland [3] has stressed the fact that the superior laryngeal nerve is only slightly above the superior thyroid artery and may thus be injured readily during ligation of the superior pole and in certain instances may give rise to changes in the vocal cords. Nordland, however, was unable to confirm the difference in positions of the two nerves which was noted by Berlin and Lahey.

Severance of the recurrent laryngeal nerve will obviously lead to paralysis of the intrinsic muscles (except the cricothyroid and possibly the interarytenoid muscle), thereby allowing the cricothyroid tensor adductor to pull the cord to the midline, with consequent obstruction to respiration, particularly if both nerves are injured. Judd and his associates [4] performed a series of experiments on dogs and noted that section and ligation of the nerve with linen would lead to permanent paralysis, whereas pinching the nerve firmly with a hemostat was followed by temporary paralysis lasting for thirty to sixty days. In general, experience teaches that practically the same results are to be expected in the human being. It should be emphasized here that paralysis of one cord, particularly if not complete, may produce no symptoms whatsoever, even in the voice, and may not be detected unless laryngologic examination is done. Detailed studies have been made by Lemere [5] on dogs showing the effect of severance of the various nerves on the glottic picture. Section of both nerves in the dogs practically always is accompanied by loss of the voice and usually, but not always, by loss of the voice in the human being.

It has been known for a great many years that anesthesia (particularly ether) produces a confusing effect on the results of stimulation of the recurrent laryngeal nerve. In 1887 Hooper [6] noted that stimulation of the recurrent nerve in dogs produced adduction of the cords under light ether anesthesia and abduction under deep ether anesthesia. Lemere [7] noted that in dogs less than 2 months old abduction is always obtained in spite of deep anesthesia, regardless of its depth. Russel [8] showed that the fibers of the recurrent nerve were divided

3. Nordland, M.: The Larynx as Related to Surgery of the Thyroid Based on an Anatomical Study, Surg., Gynec. & Obst. **51**:449, 1931.

4. Judd, E. S.; New, G. B., and Mann, F. C.: The Effect of Trauma on the Laryngeal Nerves: An Experimental Study, Ann. Surg. **67**:257, 1918.

5. Lemere, F.: Innervation of the Larynx: Experimental Paralysis of the Laryngeal Nerve, Arch. Otolaryng. **18**:413 (Oct.) 1933.

6. Hooper, F. H.: The Recurrent Laryngeal Nerves, New York M. J. **46**:29, 1887.

7. Lemere, F.: Innervation of the Larynx: IV. An Analysis of Semon's Law, Ann. Otol., Rhin. & Laryng. **43**:525, 1934.

8. Russel, J. S. R.: The Abductor and Adductor Fibers of the Recurrent Laryngeal Nerve, Proc. Roy. Soc., London **51**:102, 1892.

into two groups, one of which supplied the abductor muscles whereas the other supplied the adductor muscles. This anatomic separation will no doubt explain some of the inconsistencies known to exist regarding the effect of stimulation of nerves on the laryngeal muscles. It has been suggested that the greater concentration of lipoid granules in the abductor than in the adductor muscles may explain the early action of ether on the abductors, but it is doubtful if this is true, since in clinical experience serious paralytic effects have been encountered under other anesthetics, such as ethylene and nitrous monoxide.

In 1881 Semon [9] proposed a rule or law that in partial or incomplete destruction of the recurrent laryngeal nerve the muscles of abduction are affected first. It has been accepted by many, but not those working on the neuromuscular mechanism of the larynx. It may possibly be supported by the experiments of Semon and Horsley,[10] who showed that when the larynx is excised from an animal the abductor muscles are the first to lose their excitability to electric stimulation.

REVIEW OF EXPERIMENTS

The object of these experiments was to determine how much contraction of the trachealis muscle and intrinsic muscles of the larynx could be obtained by electric stimulation and by reflex action such as might be produced by operative trauma about the neck, particularly on the thyroid. Observations on the trachea were made by making a midline incision in the neck, with the dog under ether anesthesia, and exposing the trachea. The recurrent and pararecurrent nerves were carefully dissected away from each side, so that an incision could be made near the sternum, a tracheal cannula inserted into the distal stump and a rubber tube with a small balloon attached to the end placed in the proximal stump. The rubber tube was connected with a tambour. Although readings could be obtained by using a rubber tambour, the excursions of the lever were much wider if a cylinder type of tambour was used. Observations on the action of the vocal cords were obtained in a similar way, the balloon being inserted into the larynx from the mouth as well as from the trachea. The stimulus used was a faradic current derived from an ordinary dry cell battery inducting coil, only a small portion of the current obtainable from the two batteries being used.

When the trachealis muscle was stimulated directly with the balloon in place, there was a pronounced slow contraction of the smooth muscle

9. Semon, F.: Proclivity to Disease of Abductor Fibers, Arch. Laryng. **2**:197, 1881.

10. Semon, F., and Horsley, F.: On an Apparently Peripheral and Differential Administration of Ether on the Laryngeal Nerves, Brit. M. J. **2**:405, 1886.

type (fig. 3). The muscle apparently fatigues slowly. The frequent oscillations of the tracing lever represent respiratory movements and can be eliminated to a great extent, with no appreciable loss in accuracy of the response, by applying a variable amount of tension on the dog's tongue or larynx. The contraction can be seen readily with the naked eye (fig. 4). As the muscle contracts, it attains the shape of a roll of muscle fibers, frequently approximating the ends of the cartilaginous rings. The diameter of the trachea lessens about 2.5 mm.; most of this decrease in the lumen takes place in the lateral diameter, but there is occasionally slight shortening in the anteroposterior direction, depending somewhat on the shape of the trachea and on similar factors. As would be expected, the maximum contraction was noted in young dogs. In old dogs, palpation of the trachea would readily show a lack of elasticity of the rings, as compared to the elasticity noted in young animals. For

Fig. 3.—The two upper tracings represent the response to stimulation of the trachealis muscle in 2 different dogs. (The tambour was connected with a balloon in the trachea.) In each instance the stimulus was maintained for about fifteen seconds. Note that contraction persisted after cessation of the stimulus. The lower curve represents the response obtained by stimulation maintained for three and one-half minutes. There was a surprising lack of fatigue, as determined by the maintenance of the height of the curve. However, when the stimulus was removed there was a rather sharp drop to the normal level.

that reason young dogs must be used for such experiments on the trachea.

When the pararecurrent, or vagus, nerve was stimulated there was likewise a contraction of the trachealis muscle (fig. 5), but naturally not as pronounced as when the muscle was stimulated directly. On certain occasions irritation of the trachea, as produced by scratching the surface with a needle, will produce a contraction, but it should be emphasized that this response is obtained only occasionally. It appears to be more readily obtained when the anesthesia is light. As a matter of

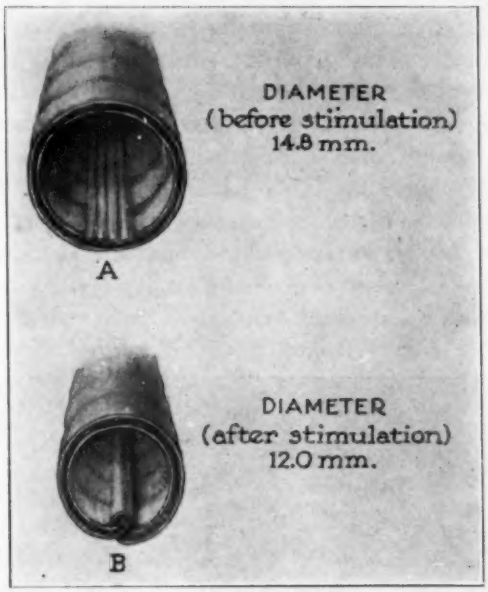

Fig. 4.—*A*, drawing of a dog's trachea, showing the slightly wrinkled trachealis muscle. *B*, drawing of same trachea while the muscle was being stimulated. Note that the muscle has contracted into a bundle, approximating (in this instance) the ends of the cartilaginous rings. The diameter changed from 14.8 to 12 mm. Contraction of this degree is obtainable only in young dogs.

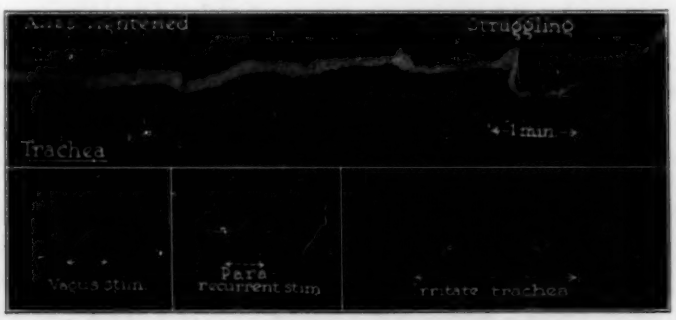

Fig. 5.—As anesthesia is lightened a marked fluctuation in tonus of the trachealis muscle (in the dog) is noted, with a tendency toward an increasing amount of spasm up to its maximum capacity. Electric stimulation of the vagus and the pararecurrent nerves produces contraction of the trachealis muscle, as would be expected. Likewise irritation of the trachea (scratching with a needle) produced a marked spasm, but this result is obtained only occasionally and is no doubt greatly dependent on the depth of anesthesia, being more active under light anesthesia.

fact, changing the depths of anesthesia without an additional stimulus will invariably result in a marked change in the size of the tracheal lumen; the most constant change is constriction of the trachea during the period when the anesthesia is being lightened. With the balloon in the larynx, spasm of the vocal cords can likewise be demonstrated during fluctuations in depth of anesthesia, particularly when the anesthesia is lightened (fig. 8).

As would be expected, with the balloon in the larynx, crushing the recurrent nerve resulted in laryngeal constriction (fig. 6); presumably the tonus of the cricothyroid muscle (innervated by the superior laryngeal nerve) with consequent adduction of the vocal cord is the factor producing the constriction. Manipulation of the nerve produced a

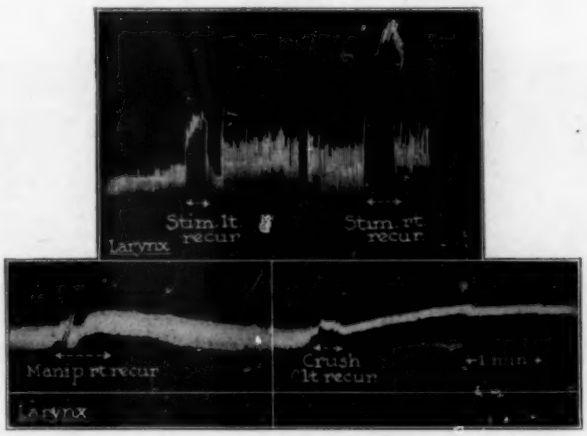

Fig. 6.—With the balloon in the larynx, electric stimulation of the recurrent nerve, under usual circumstances, produces a bilateral adductor (see text) spasm. In this experiment manipulation induced a mild adductor spasm and crushing the nerve a more pronounced spasm, as would be expected. Crushing the recurrent nerve paralyzes it, thus affecting the adductor as well as abductor fibers within it and allowing the cricothyroid muscle, which is innervated by the superior laryngeal nerve, to adduct the cord by its tensor action. It is obvious then that if any effect is produced most types of stimulation or trauma are likely to result in an adductor spasm.

spasm of less intensity; this response is by no means constant and is only mild. It has been observed in human beings by laryngoscopic examination (Curtis [11]). However, during manipulation of the nerve incident to total thyroidectomy Seed [12] has not noted sufficient adductor spasm

11. Curtis, G.: Personal communication to the author.
12. Seed, L.: Personal communication to the author.

to produce stridor. Stimulation of the recurrent nerve results primarily in adduction of the cords, but circumstances may occasionally result in abduction. This seemingly paradoxic reaction is made possible by the fact that the nerve contains abductor as well as adductor fibers (Russel [6]); their threshold of response to stimuli appears to be variable. The sharp adductor spasm which is so commonly obtained has been noted by numerous observers and may involve both cords. Fishman [13] showed experimentally that the bilateral action was peripheral as well as central by obtaining the same response (bilateral spasm) under stimulation of one recurrent nerve when the other was severed. He remarked that this did not necessarily prove that there was a chiasmic innervation but was of the opinion that the stimuli reached the other side by crossing nerve fibers of peripheral synapses. The strong adductor action proves that the adductor muscles, at least in this instance, were stronger

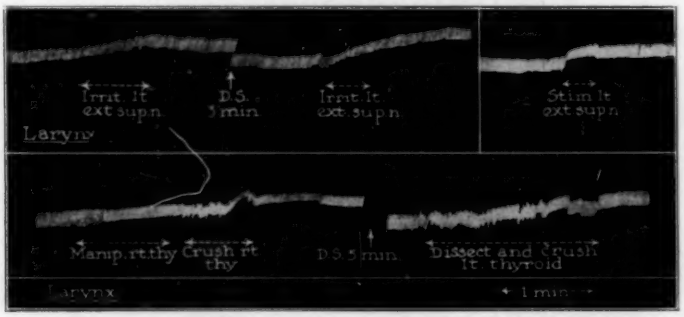

Fig. 7.—Irritation of the external superior laryngeal nerve usually produces a mild adductor spasm of the cords. In this experiment the drum was stopped for three minutes (indicated by *D. S.*) to allow the nerve and muscles to recover. Electric stimulation of the nerve likewise results in adductor spasm. In this experiment manipulation and crushing the thyroid produced an adductor spasm. However, this response is by no means constant and apparently occurs in the animal only when the anesthesia is light.

than the abductor, or that the cricothyroid muscles, which are innervated by the superior laryngeal nerve, were stimulated by reflex or by an overflow of stimuli.

Irritation and stimulation of the external superior laryngeal nerve produce laryngeal constriction (fig. 7). Manipulation and crushing of the thyroid may produce no demonstrable effect on the tonus of the laryngeal muscles, but occasionally (fig. 7) a definite laryngeal constriction is produced. This result is, of course, comparable to the

13. Fishman, L. Z.: Personal communication to the author.

adductor spasm which is occasionally noted during thyroidectomy when clamps are applied to certain parts of the thyroid, even though this area is a considerable distance from the recurrent nerve itself. The action is undoubtedly reflex.

As stated previously, conflicting results are occasionally obtained, and since the early work of Semon and Hooper they have been the subject of much dispute. The sharp relaxation of the cords demonstrated in figure 8 by traumatizing the trachea (crushing the edge with a hemostat) is an example of an inconsistent result. There appears to be no decisive explanation.

COMMENT

An analysis of the experiments reveals that the trachealis muscle (at least in the dog) is capable of a definite contraction. Stimulation of

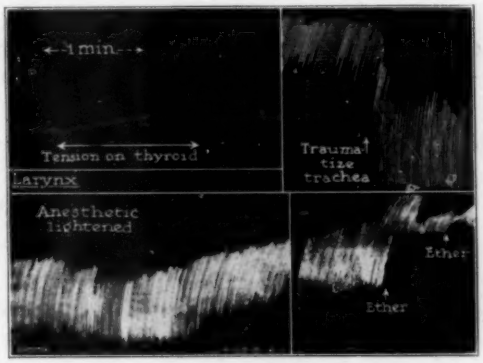

Fig. 8.—Occasionally tension on the thyroid will produce an adductor spasm of the vocal cords. The sharp abductor response obtained by traumatizing the dog's trachea (crushing the edge with a hemostat) appears paradoxic; abductor response of this type was obtained rarely in the experiments performed in this report. The adductor spasm produced by lightening the anesthesia or by suddenly increasing the amount of ether given is a response well known to all.

the muscle itself produces a greater contraction than stimulation of the pararecurrent nerve but to a degree which decreases the diameter of the trachea no more than 2.5 or 3 mm. The contraction produced by reflex stimuli did not approach this in intensity except perhaps during the struggling incident to a lightening of the anesthetic. A narrowing of the trachea to a degree greater than that mentioned is prevented by contact of the tip of the cartilaginous rings and by the support afforded by the horseshoe-shaped rings themselves. Obviously if through abnormality of some type or other the support of the rings is lost, an

actual collapse would be possible. Colp and Louria [14] found that resection of at least seven rings was necessary in dogs before an obstructive collapse was produced. In the human being the cartilaginous support may be lost either through constitutional disease or through pressure atrophy produced by an adenoma of the thyroid. The elasticity of the trachea minimizes the effect of pressure by an adjacent nodule of thyroid but numerous proved instances of tracheal collapse of this type have been reported (Peterson and Rovenstine,[15] Henry,[16] Moersch [17] and others). The patient reported on by Moersch had stridor immediately after operation, but tracheotomy was not necessary until the fourth postoperative day. Bronchoscopic examination revealed an absence of tracheal rings and collapse of the lateral walls of the trachea. Every one is acquainted with the serious obstructive effect of a postoperative hemorrhage. Even after evacuation of the blood clot there may be sufficient edema and infiltration of the mucous membrane to make tracheotomy necessary, as has been noted by Rosenblatt.[18]

Additional experiments were carried on to determine whether or not the negative pressure developed in the respiratory passages by forced inspiration in the presence of a laryngeal obstruction might produce occlusion of the trachea. The trachea and larynx were removed from 10 patients at autopsy, and the trachea was subjected to a negative pressure of 70 mm. of mercury. In one instance there was complete collapse of the tracheal wall at a negative pressure as low as 20 mm. of mercury (fig. 9*A*). This patient died of pancreatic asthenia and pronounced fatty infiltration of the liver; the disease process was probably instrumental in the loss of the normal stiffness in the cartilaginous rings. In no other instance did such a pronounced collapse of the trachea take place in my experiments with negative pressure; in fact, the average decrease in the lateral diameter when the interior of the trachea was subjected to a negative pressure of 70 mm. of mercury was only 3 mm. Macleod [19] gives 100 mm. of mercury as the maximum positive pressure developed during forced expiration and 70 mm. of mercury as the negative pressure during forced inspiration. For that reason no

14. Colp, R., and Louria, H. W.: Dyspnea Following Thyroid Operation, Arch. Surg. **11**:200 (Aug.) 1925.

15. Peterson, M. C., and Rovenstine, E. A.: Tracheal Collapse Complicating Thyroidectomy, Anesth. & Analg. **15**:300, 1936.

16. Henry, C. K. P.: Tracheal Collapse During Thyroidectomy, Anesth. & Analg. **6**:146, 1927.

17. Moersch, H. J.: Tracheal and Esophageal Compression as a Result of Adenomatous Goiter, Ann. Otol., Rhin. & Laryng. **40**:909, 1931.

18. Rosenblatt, M. S.: Tracheotomy After Thyroidectomy, Northwest Med. **28**:330, 1929.

19. Macleod, J. J. R.: Physiology in Modern Medicine, St. Louis, C. V. Mosby Company, 1930.

negative pressures greater than 90 mm. of mercury were used. It is possible that if a spasm of the trachealis muscle were present, a greater narrowing of the trachea would be possible, but the resistance of the rings would prevent total collapse unless atrophy of the rings were present. In fact, it is probable that a more pronounced obliteration of the lumen of the trachea would result if it were submitted to a negative pressure of forced inspiration with the larynx blocked and with the trachealis muscle relaxed, so that it could protrude anteriorly into the lumen as shown in figure 9 *A*.

During the course of the preceding experiments it was noted that the stimuli producing a spasm of the adductor muscles of the larynx or of the trachealis muscle were similar. In fact, there was a decided

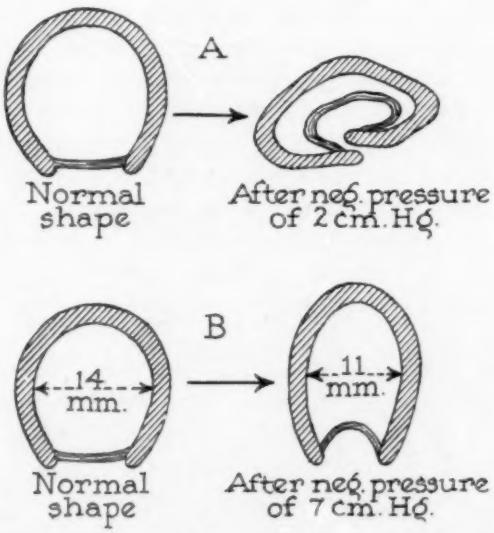

Fig. 9.—*A* represents an almost total collapse of the trachea (of a human being) as produced by a negative pressure of 2 cm. of mercury in a trachea removed at autopsy. This amount of collapse is uncommon. The patient died of pancreatic asthenia and fatty degeneration of the liver. The tracheal rings were undoubtedly abnormal so far as they had lost their normal support. *B* represents the average influence of a pressure of —7 cm. of mercury on 9 other tracheas removed at autopsy from patients dying from various causes. The diameter has been narrowed only 3 mm.

tendency for the spasm to effect the trachea and the larynx simultaneously. The larynx is more susceptible, and naturally muscular spasms involving it are more important than changes in the trachea, particularly since complete collapse of the trachea is not possible in a normal trachea and since in spasm of the larynx the adductors predominate, thereby producing obstruction. It was found that various

stimuli, such as crushing or manipulation of the thyroid or irritation of the trachea or recurrent laryngeal nerves, would produce adductor spasm. It is probable that in many instances the obstruction is produced by spasm of the adductors, whereas in other instances the adductor action is produced solely by muscle tonus in the presence of paralysis of the abductors. The tendency of the abductors to become paralyzed long before the adductors as the result of mild trauma (Semon's law) has been supported by many observers. This simple phenomenon in certain instances might explain the predominance of the adductors over the abductors in the case of trauma. However, in many instances the adduction of the vocal cords is no doubt primarily a reflex resulting from stimulation by irritation or trauma; in this instance the adductors as well as the abductors might be stimulated, but the more powerful adductors would control the action of the cords. When this reflex stimulation takes place, the resultant effect would likewise be likely to be bilateral. This effect on both sides, as stated previously, is thought to be produced through a direct crossing of stimuli at the periphery (i. e., within the larynx) and, as Fishman has emphasized, may not be the result of another reflex of central origin.

One of the most pronounced spasms noted during the course of the experiments described was observed when the femoral vein was isolated preparatory to an intravenous injection. The trauma incident to the isolation of the vein, consuming perhaps five or ten seconds, was the inciting factor.

The causes of adductor spasm of the larynx as noted clinically are too numerous to attempt to enumerate. Paralyses occurring as long as several weeks or months after thyroidectomy, presumably through the action of compression of the nerve by scar, have been reported. More commonly this delayed reaction is noted a few hours or a day or two after operation and in such instances is produced by excessive edema of the structures surrounding the recurrent nerve or by infiltration of that area by blood, thereby resulting in compression of the nerve. Several years ago I observed a patient with a large substernal goiter who was able to talk normally for twelve hours after thyroidectomy, but serious stridor gradually developed until tracheotomy was necessary twenty-four hours after operation. At the time of the tracheotomy a hemorrhage into the tissues on the floor of the operative field on each side was noted, but little blood clot was present in the wound itself. In this instance it appears likely that the infiltration of the tissues in the floor of the operative field had involved the recurrent nerve on each side, thereby resulting in paralysis of the vocal cords with consequent laryngeal obstruction.

The paralyses described in the foregoing paragraph may be considered as being mechanical in origin. However, temporary paralyses

of reflex origin are much more common. Anesthetists are aware of the frequency of laryngeal spasm and look on it as being one of the most important obstacles in obtaining smooth anesthetics. In fact, some anesthetists (Sise [20] and others) feel that laryngeal spasm is so troublesome that they use intratracheal anesthesia for laparotomies and similar operations, so that closure of the glottis cannot take place. Brewer [21] and his associates showed experimentally that traction on the mesentery or stimulation of the splanchnic nerve with the faradic current resulted in cessation of breathing with closure of the glottis by adductor spasm of the vocal cords. They offered additional proof of this reflex effect by obtaining action potentials from one of the recurrent laryngeal nerves while visceral traction or electric stimulation was performed.

SUMMARY

After consideration of the problem, it was concluded that the obstruction to respiration as sustained by the patient described in this report resulted from reflex closure of the glottis (adductor spasm approximating the vocal cords). The stimulus producing this action may have been produced by the application of clamps on the capsule of the gland or by pulling on the thyroid lobe, which may or may not have resulted in tension on the recurrent laryngeal nerve on that side. The spasm undoubtedly involved both sides. Experimental support for these explanations are presented. The fact that the patient recovered on the operating table without any hemostats being removed from the region of the nerve would appear to prove that actual trauma to the nerve had nothing to do with the action unless it was tension on the nerve.

The trachealis muscle is capable of considerable contraction either by direct stimulation or by reflex action. The elastic resistance of the cartilaginous bars prevents a decrease in diameter of more than 3 mm. unless an erosion of the rings is present (as may be produced by compression from an adenoma of the thyroid) or a loss in strength of the rings is created by constitutional disease. True complete tracheal collapse therefore cannot occur in a normal human trachea.

The decrease in diameter of the trachea as observed in the operation mentioned could be explained on the basis of a spasm of the trachealis muscle or a partial collapse incident to obstruction produced by adductor laryngeal spasm or both. The latter factor would appear to be more

20. Sise, L. F.: Choice of Anesthesia for Surgery of the Upper Abdomen, Am. J. Surg. **40**:22, 1938.

21. Brewer, N.; Luckhardt, A. B.; Lees, W. M., and Bryant, D. S.: Reflex Closure of the Glottis by Stimulation of Afferent (Visceral) Fibers, Anesth. & Analg. **13**:257, 1934. Brewer, N., and Bryant, D. S.: The Role of the Splanchnics in the Adductor Spasm of the Vocal Cords Following Visceral Traction, ibid. **14**: 190, 1935.

significant. This amount of change in size of the caliber of the trachea is undoubtedly rare as a complication of thyroidectomy.

Obstruction created by adductor spasm of the larynx with approximation of the cords is a much more significant cause of respiratory difficulty than obstruction in the trachea, not only during thyroidectomy but during most other operations as well. This spasm is reflex and can be produced experimentally by such methods as tension on the thyroid, crushing and manipulation of the thyroid, trauma to blood vessels, lightening of anesthesia or sudden administration of an anesthetic (ether). Most of the reflex obstructions produced experimentally by the aforementioned methods are obtained only occasionally and in that respect resemble clinical experiences.

Undoubtedly, the fact that the recurrent nerve contains adductor and abductor fibers, as pointed out by Russel,[8] is of considerable assistance in explaining why various stimuli (whether reflex or otherwise) result so commonly in adductor spasm of the larynx, particularly since the adductor muscles are obviously much stronger than the abductor. The nerve fibers going to the abductors of the larynx are larger than those going to the adductor.[7] Although large fibers are more excitable [22] than smaller fibers, by the recognized neurologic principles they should likewise be less resistant to trauma. The fact that the abductor muscles lose their power to respond to electric stimulation before the adductor, as determined at autopsy on human beings [23] and by experiments on the excised larynx of the dog,[24] would likewise be of significance in explaining why adductor action results so commonly in the laboratory and operating room when trauma serves as the source of the stimuli.

Experiments described in this report indicate that the respiratory obstruction sustained by the patient herein reported on what was caused by reflex adductor spasm of the larynx. A large proportion of tracheotomies performed for respiratory obstruction during thyroidectomy are done for this condition. Proof of this statement will be at hand if it is possible to remove the tracheotomy tube within a day or two after tracheotomy.

If significant respiratory stridor is encountered when the surgeon is positive that the recurrent nerve has not been injured, he should immediately stop the operation, release all tension on the thyroid and remove any pressure such as might be inflicted by weight of hemostats. Tracheotomy is naturally to be avoided as far as possible, particularly

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22. Gerard, R. W.: Nerve Conduction in Relation to Nerve Structure, Quart. Rev. Biol. **6**:59, 1931.

23. Jeanselme, D., and Lermoyez, M.: Etude sur la contractilité post mortem et sur l'action de certains muscles, d'apres des expérimentes faites sur des cadavres de cholériques, Arch. de physiol. norm. et path. **6**:109, 1885.

24. Lemere.[7] Semon and Horsley.[10]

since the entire wound in such instances usually becomes infected. The insertion of a catheter through the larynx into the trachea will obviously combat the obstruction effectively. In such instances it may be impossible to remove an intratracheal catheter or tracheotomy tube for several days.

The depth of anesthesia is undoubtedly important in the causation and treatment of laryngeal spasm. In the first place it will occur much less frequently under local anesthesia. If the patient is anesthetized deeply before the operation is begun, laryngeal spasm will be much less likely to develop. If stridor develops during the operation, for which light anesthesia is being used, putting the patient into a deeper stage of anesthesia will usually correct it, but rarely so unless the operator ceases all manipulation. On numerous occasions, however, deepening the anesthesia will be of no avail; moreover, if the stridor is severe and develops rapidly, the anesthetist will probably be fearful of any attempt to deepen it. Regardless of whether the anesthesia is lightened or deepened in an attempt to control the stridor, it will obviously be necessary to administer a mixture high in oxygen content. As pointed out by Lahey,[25] helium should always be administered with the oxygen because of its effect of increasing the flow of oxygen through the narrowed glottic aperture.

It must of course be appreciated that an actual mechanical obstruction of the trachea may be produced during thyroidectomy by careless manipulation of the thyroid lobes, particularly if they are large and extend posteriorly. If a softening or atrophy of several tracheal rings has taken place because of compression by an adenoma, no amount of care may prevent obstruction at this point because of collapse of the walls of the trachea.

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25. Lahey, F.: Modern Development in Anesthesia and Anesthetists, South. M. J. **31**:29, 1938.

TUMOR OF THE HYPOPHYSIAL DUCT (RATHKE'S CYSTS)

REPORT OF ELEVEN CONSECUTIVE CASES

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A congenital tumor arising from an embryologic rest in the region of the pituitary body and the sella turcica is rarely encountered even in a large neurosurgical clinic, but the occurrence is sufficiently frequent to warrant consideration of such a tumor in the differential diagnosis of the cause of disturbance of vision in a child or a young adult. Particularly is this true if the patient's vision cannot be improved with corrective lenses or if there is edema of the optic disks as observed on funduscopic examination. The diagnosis of a tumor in the chiasmal region usually is not difficult if the condition is considered as a possibility.

Cases of intracranial tumor arising from a residual cell rest of the primitive hypophysial duct were reported as early as the latter part of the nineteenth century. The early reports were based on both operative material and material obtained at necropsy. In spite of the excellent anatomic, pathologic and clinical studies which have been derived from such sources, adequate attention has not been paid to the surgical problem presented by cases of this type.

This report is based on a careful analysis of the records of 11 consecutive cases in which the clinical diagnosis was verified surgically and in which there was neither operative nor subsequent mortality.[1] The patients were operated on by one surgeon (J. G. L.), and this explains the small number of patients with this type of tumor seen in such a relatively long period. Cases in which this type of tumor was observed by Adson and Craig during the same period (April 1935 to Jan. 28, 1938) were not included in this study. In view of the unusually fortu-

From the Section on Neurologic Surgery, the Mayo Foundation (Drs. Love and Shelden), and the Section on Pathologic Anatomy, the Mayo Clinic (Dr. Kernohan).

1. One patient was killed in an automobile accident one and one-half years after operation.

nate results, both operative and postoperative, this series of cases was considered important enough to be subjected to critical study in an effort to determine what measures were undertaken which might influence the mortality rate in cases of this serious intracranial lesion. Lesions of the hypophysial duct are the source of one of the most formidable challenges presented by tumors involving the central nervous system.

The acquisition of knowledge as to the exact mode of origin of the hypophysis cerebri and as to the significance of the squamous epithelial cell rests from which tumor of the hypophysial duct arises has been slow and tedious. Rathke [2] in 1838 was the first to assert that the pituitary body developed from a diverticulum of the pharynx. Some years later (1857) Zenker [3] observed squamous epithelial cysts in the region of the optic chiasm but did not fully appreciate their significance or their importance in the production of intracranial tumor.

The relative rarity of tumor of the hypophysial duct is illustrated by the infrequency of reports of cases of this lesion. The high operative mortality probably accounts to some extent for the scarcity of articles on the subject. Up to 1916, when Jackson [4] reported a collected series of 38 cases of tumor arising from remnants of the hypophysial duct, reports of cases had appeared sporadically and had been based almost entirely on postmortem material. Duffy [5] in 1920 was able to add 18 cases, gathered chiefly from a more careful perusal of the literature, thus bringing the number of reported authentic cases at that time to the rather small total of 56.

Since that date, tumors of this type have been observed and reported with much greater frequency; nevertheless, they continue to represent a very small percentage of chiasmal tumors and constitute a group worthy of intensive study, especially from the standpoint of proper surgical management.

In the past, as at the present time, much confusion was evident in regard to the proper designation of this type of tumor. It has been described under a great variety of names, depending apparently on the personal points of view and interests of the authors. Histologically it has been classified as adamantinoma; anatomically as interpeduncular or suprasellar cyst, and embryologically as Rathke's cyst, craniopharyn-

2. Rathke, cited by von Mihalkovics, V.: Wirbelsaite und Hirnanhang, Arch. f. mikr. Anat. **11**:389-441, 1875.

3. Zenker, cited by Erdheim, J.: Pathologie der Hypophysengeschwülste. Ergebn. d. allg. Path. u. path. Anat. **21**:482-561, 1926.

4. Jackson, H.: Craniopharyngeal Duct Tumors, J. A. M. A. **66**:1082-1084 (April 8) 1916.

5. Duffy, W. C.: Hypophyseal Duct Tumors: A Report of Three Cases and a Fourth Case of Cyst of Rathke's Pouch, Ann. Surg. **72**:537-555 (Nov.); 725-757 (Dec.) 1920.

gioma and tumor of the hypophysial duct. As will be shown later, it may vary greatly in its gross and histologic appearance as well as in its exact situation. However, all instances have in common the development from squamous epithelial cell rests which are remnants of the embryonic hypophysial duct, and consequently it appears logical to designate such a growth as a tumor of the hypophysial duct.

EMBRYOLOGY

The hypophysis cerebri is developed by the union of two portions, one an outpouching of the wall of the third ventricle, forming the neural posterior lobe, the other an outpouching from the *Rachenepithelium* of the primitive buccal cavity, forming the glandular anterior lobe.

The history of the development of the pituitary body makes a most interesting chapter in embryology, the details of which are vital to a clear understanding of the problem of tumor of the hypophysial duct. Müller [6] in 1871 and Mihalkovics [7] in 1875 are generally given credit for having first presented accurate and complete descriptions of the intricate embryonic mechanism [8] whereby the adult pituitary body develops from the primitive buccal cavity.[9]

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6. Müller, W., cited by Atwell.[9a]

7. von Mihalkovics, V.: Wirbelsaite und Hirnanhang, Arch. f. mikr. Anat. **11**:389-441, 1875.

8. For a more detailed embryologic description, one may consult the thesis submitted to the University of Minnesota by Dr. C. Hunter Shelden.

9. (*a*) Atwell, W. J.: The Development of the Hypophysis Cerebri of the Rabbit (Lepus Cuniculus L.), Am. J. Anat. **24**:271-337 (Sept.) 1918. (*b*) Carmichael, H. T.: Squamous Epithelial Rests in the Hypophysis Cerebri, Arch. Neurol. & Psychiat. **26**:966-975 (Nov.) 1931. (*c*) Erdheim, J.: Pathologie der Hypophysengeschwülste, Ergebn. d. allg. Path. u. path. Anat. **21**:482-561, 1926. (*d*) Frazier, C. H., and Alpers, B. J.: Tumors of Rathke's Cleft (Hitherto Called Tumors of Rathke's Pouch), Arch. Neurol. & Psychiat. **32**:973-984 (Nov.) 1934. (*e*) Goette, cited by Duffy.[5] (*f*) Harbitz, F.: Tumours Arising from the Hypophyseal Duct, and Other Neoplasms Related Thereto; Chordomas, Acta path. et microbiol. Scandinav. **12**:38-78, 1935. (*g*) Kiyono, H.: Ueber das Vorkommen von Plattenepithelherden in der Hypophyse, Virchows Arch. f. path. Anat. **252**:118-145, 1924. (*h*) Luschka, cited by Atwell.[9a] (*i*) McLean, A. J.: Die Craniopharyngealtaschentumoren (Embryologie, Histologie, Diagnose und Therapie), Ztschr. f. d. ges. Neurol. u. Psychiat. **126**:639-682, 1930. (*j*) Rasmussen, A. T.: Ciliated Epithelium and Mucus-Secreting Cells in the Human Hypophysis, Anat. Rec. **41**:273-282 (Feb.) 1929. (*k*) Susman, W.: Embryonic Epithelial Rests in the Pituitary, Brit. J. Surg. **19**:571-576 (April) 1932. (*l*) Tilney, F.: An Analysis of the Juxta-Neural Epithelial Portion of the Hypophysis Cerebri, with an Embryological and Histological Account of a Hitherto Undescribed Part of the Organ, Internat. Monatschr. f. Anat. u. Physiol. **30**:258-293, 1914. (*m*) Waterston, D.: The Development of the Hypophysis Cerebri in Man, with a Note upon Its Structure in the Human Adult, Tr. Roy. Soc. Edinburgh **55**:125-145 (May 20) 1927. (*n*) Ewing, J.: Neoplastic Diseases, ed. 2, Philadelphia, W. B. Saunders Company, 1922.

SITUATION

On theoretic grounds alone, one might expect to find that tumor of the hypophysial duct develops at any point along the course of the primitive hypophysial duct; however, clinically it is rarely found extracranially. Frequently typical groups of cell rests have been found in the region of the vomer and the sphenoid sinus, but they apparently do not result in the formation of a tumor, or if they do they do not produce symptoms. The favorite site of origin of tumor of the hypophysial duct is in the midline above the sella turcica, in the infundibular region along the hypophysial stalk or beneath the optic chiasm. It may develop either above or below the diaphragm or dural roof of the sella; however, in many instances it produces early rupture of this membrane, and then accurate anatomic localization may be impossible.[10] Thus, it is seen that the tumor develops most frequently from the region of the infundibulum and from the anterior superior aspect of the capsule of the anterior lobe of the pituitary body, a site which corresponds to that at which epithelial cell rests are found in a high percentage of normal [11] pituitary bodies.

GROSS APPEARANCE

Tumor of the hypophysial duct varies in gross appearance from a small, solid, well circumscribed, discrete growth to a huge, multilocular cyst producing marked displacement of the adjacent structures. The capsule is in many instances smooth and white and of sufficient density to tolerate considerable manipulation without tearing; however, it may be thin and fragile and may have a dark appearance as a result of the color of the contained fluid.[12] If the tumor is of long standing or has developed with great rapidity it may infiltrate the surrounding tissue to such an extent that surgical dissection of the lesion from the adjacent structures is impossible. Although the tumor is generally solid in its early stages, it soon undergoes cystic degeneration; the fluid content of the cyst is usually yellowish, dark brown or greenish brown, and there often is as much as 2 to 3 ounces (60 to 90 cc.) of this fluid. Generally, the fluid contains crystals of cholesterol, which are clearly visible floating on the fluid as the cystic cavity is opened. Calcification is usually present

10. Cushing, H.: Intracranial Tumors, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

11. Bartels, P.: Ueber die Beziehungen von Veränderungen der Hypophysengegend zu Misswachstum und Genitalstörungen (Dystrophia adiposo-genitalis), München. med. Wchnschr. **55**:201-202 (Jan. 28) 1908.

12. Dandy, W. E.: The Brain, in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1932, pp. 598-605.

in the lesion and is said by some authors to be demonstrable roentgenographically in 85 per cent of cases.[13] The amount of calcium present may vary from that which produces minute local areas of calcification above the sella turcica to that which produces a definite line of calcification completely outlining the entire extent of the tumor (fig. 1). Extreme degrees of calcification (fig. 2) have been reported, in which the entire tumor became stony hard, so that it was impossible to section it by routine methods for microscopic studies.[14]

HISTOLOGIC APPEARANCE

The microscopic appearance of tumor of the hypophysial duct is as variable as the gross appearance.[15] The criterion for diagnosis, accord-

Fig. 1 (case 5).—Lateral roentgenogram of the head, showing diffuse calcification in the midline at the outlet of the sella turcica and partial destruction of the dorsum sellae.

ing to Critchley and Ironside,[16] is the presence of a single row of columnar cells which correspond in structure to the embryonic ameloblasts and which are arranged in palisade formation at the periphery of the epithelial masses.

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13. McKenzie, K. G., and Sosman, M. C.: The Roentgenological Diagnosis of Craniopharyngeal Pouch Tumors, Am. J. Roentgenol. **11**:171-176 (Feb.) 1924.

14. Bailey, P.: Note Concerning Keratin and Keratohyalin in Tumors of the Hypophyseal Duct, Ann. Surg. **74**:501-505 (Oct.) 1921.

15. Frazier, C. H., and Alpers, B. J.: Adamantinoma of the Craniopharyngeal Duct, Arch. Neurol. & Psychiat. **26**:905-965 (Nov.) 1931.

16. Critchley, M., and Ironside, R. N.: The Pituitary Adamantinomata, Brain **49**:437-481 (Dec.) 1926.

The outer row of cells lying on a basement membrane is the most constant histologic feature. These cells are long and slender; they have oval, elongated, deeply stained nuclei and are so situated that the long axis of each is approximately at right angles to the underlying basement membrane [16] (fig. 3).

The intermediate zone is generally less distinct than the outer zone and frequently is absent. The cells which constitute this area are roughly similar to those of the peripheral zone but are less elongated and less uniform in appearance.

The innermost area of the epithelial masses constitutes the stellate zone. This portion of the epithelial column appears as a fine, cobweb-like reticulum in which are enmeshed scattered, loosely arranged cells.

Fig. 2.—Lateral roentgenogram of the head of a 7 year old child, showing an extreme degree of calcification in what was considered to be a tumor of the hypophysial duct. The child was blind but had no other symptoms at the time of examination. In addition to the erosion of the sella turcica, one may note the separation of the cranial sutures and the erosion of the calvarium secondary to increased intracranial pressure.

They stain less intensely than the closely packed peripheral columnar layer of cells, and the nuclei, which are large and vesicular, frequently have a crescentic arrangement. This formation is often seen within the epithelial whorls commonly encountered in the stellate zone. The whorls closely simulate those characteristically found in squamous cell epithelioma. The central portions of these whorls probably undergo hyalinization or keratinization and later calcification, which accounts for the frequent presence of masses of calcium in the central areas of the whorls. Generally, the stroma or supporting structure is fibrous tissue

arranged irregularly among the epithelial columns. However, the pattern is dominated by two rather constant types. In one the fibrous tissue is present as fine strands with a lacelike appearance. The other type consists of coarse, dense fibrous tissue with narrow slitlike interspaces.

Occasionally the epithelial masses are completely surrounded by neuroglia, and sometimes neuroglia is completely absent. Usually, examination of the glial tissue does not reveal any histologic evidence of reaction to the growth of the adjacent tumor.

Degeneration associated with cyst formation is a conspicuous feature of tumor of the hypophysial duct. In addition to true cysts, there are

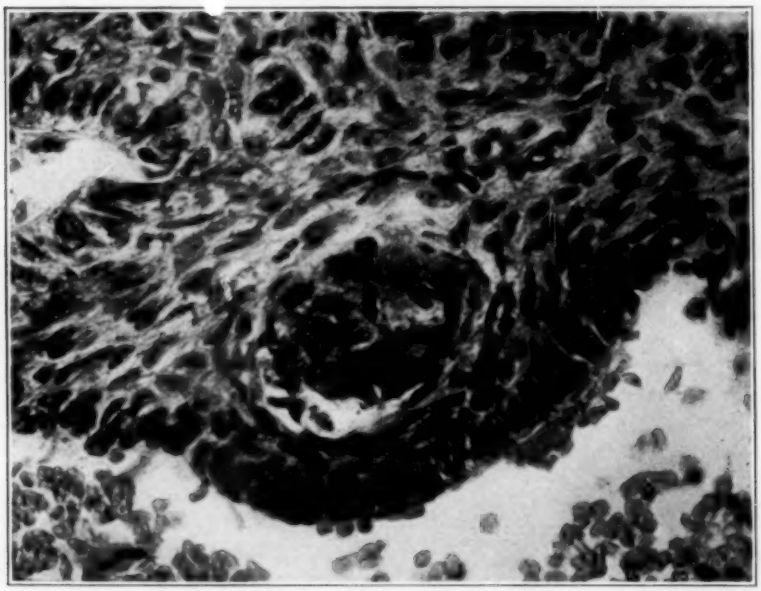

Fig. 3.—Palisade formation of the elongated columnar cells forming the ameloblast layer; a definite basement membrane is demonstrated; the specimen is stained with hematoxylin and eosin (× 450).

numerous slits or prism-shaped empty spaces, which represent former sites of cholesterol crystals in the tissue. Fresh sections examined under the polariscope reveal these refractile crystals.[17] Bailey [18] said that calcium is visible microscopically in every tumor of the hypophysial duct. In our cases the area of calcification varied in size from minute,

17. Footnote deleted by authors.

18. Bailey, P.: Intracranial Tumors, Springfield, Ill., Charles C. Thomas, Publisher, 1933.

discrete particles to large, irregular calcified masses. About the cholesterol crystals and masses of calcium large foreign body giant cells not infrequently are seen.

Intercellular bridges are common in fresh sections stained by the polychrome methylene blue method. Keratohyaline granules frequently have been reported in tumor of the hypophysial duct,[14] but such granules were not observed in this series of cases.

A striking feature of the histologic appearance of the tumor is its extreme avascularity. This may in part account for the readiness with which the tumor undergoes diffuse degeneration, with cyst formation.

The presence of visible bone in sections of the tumors has been reported consistently in the literature. In spite of a careful search, no such material was observed in this particular series.

CHARACTERISTIC PATHOLOGIC CHANGES

Tumor of the hypophysial duct must be distinguished from several closely related but histologically dissimilar tumors of embryonic origin. Dermoid and epidermoid tumor not infrequently occur adjacent to the sella turcica; when either tumor occurs above the tentorium cerebelli the origin usually is in the basofrontal region. An epidermoid tumor is one in which only squamous and basal epithelium are present. A tumor which, in addition, contains other elements of normal skin, such as sweat glands, sebaceous glands or hair follicles, is considered a dermoid tumor.[19]

Histologically the criterion for diagnosis of an epidermoid tumor is the demonstration of definite squamous epithelium. Keratohyaline granules, intercellular bridges and cornification are prominent features. In fact, it is the desquamation of the cornified cells which produces the main bulk of the contents of these cysts. When other elements of normal skin are present in addition to the squamous epithelium, the tumor is a dermoid. On rare occasions all three germ layers may be represented in the same tumor, which is classified as a teratoma.

SYMPTOMS

In cases of tumor of the hypophysial duct, as in cases of any other lesion presenting such a wide and bizarre range of gross characteristics, the symptoms do not follow a stereotyped pattern but depend on the size and rate of growth of the tumor as well as on the order in which the adjacent structures are involved.

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19. Love, J. G., and Kernohan, J. W.: Dermoid and Epidermoid Tumors (Cholesteatomas) of the Central Nervous System, J. A. M. A. **107**:1876-1883 (Dec. 5) 1936.

Importance has been placed on the exact site of origin of the tumor in relation to the dural roof of the sella turcica as a determining factor in the developmental sequence of the clinical symptoms.[20] A tumor which develops from epithelial cell rests situated below the diaphragma sellae naturally compresses first the pituitary body and later extends upward to involve the cephalad structures. As this type of lesion expands upward, it must push the dural roof before it; hence, signs of pituitary dysfunction may long antedate other symptoms. Such a lesion, because of its anatomic situation, may be considered an epidural growth, and it has been suggested [20] that in many instances long-standing mild headache may be the result of gradual upward stretching of this portion of the dura rather than a low grade hydrocephalus.

A tumor arising above the dural roof of the sella turcica has its origin in cell rests situated along the stalk of the infundibulum and the anterior superior aspect of the capsule of the pituitary body. Naturally, such a growth is within the subarachnoid space, and it early tends to fill the cisterna basalis. A tumor of this type tends to produce early involvement of the visual pathways and of the hypothalamus, whereas the element of pituitary dysfunction is not marked, because the lesion is separated from the pituitary body by the diaphragma sellae.

If the tumor originates from rests situated at the point of passage of the stalk through the dural roof, rapid growth of the mass may cause simultaneous functional changes in structures both above and below the diaphragma sellae.

The symptoms may be further altered from any given pattern by a sudden hemorrhage into a large cystic cavity or by a rapid local degenerative process which produces irritant material that initiates a local or diffuse inflammatory process in the suprasellar region.[20]

The symptoms of tumor of the hypophysial duct have been described very well by Cushing.[10] They may be the result of pituitary dysfunction, visual disturbance, hypothalamic compression or increased intracranial pressure associated with hydrocephalus. Generally the initial symptoms are either visual or pituitary, but if the lesion is allowed to progress to a sufficient size the majority of the classic symptoms will be present.

Pituitary involvement results in degrees of dysfunction varying from mild, easily overlooked hypopituitary states to obvious dystrophia adiposogenitalis. The endocrine disturbances are generally evidenced by the Fröhlich type of physical appearance; however, the Lorain type of

20. Wittermann, E.: Hypophysengangtumoren und vegetative Zentren des Zwischenhirns, Nervenarzt **9**:441-453 (Sept.) 1936.

infantilism without adiposity occasionally is observed.[21] Critchley and Ironside [16] mentioned the frequency of the association of acromegaly with an intrasellar growth of this type, but this is contrary to our experience. Neither acromegaly nor gigantism was observed in any of the cases in this series.

Cachexia is one of the less frequent manifestations of pituitary dysfunction; it has been observed by some authors in cases of tumor of the hypophysial duct,[22] but it did not occur in any of our cases. In case 8 mild menstrual irregularity, which was first noticed eight years before the patient came to the clinic, was the first symptom; the subsequent amenorrhea antedated the onset of headache and vomiting by more than two years. In case 3 the patient, who was a man aged 31, had noted an unusual, feminine distribution of pubic hair and a pale and pasty complexion for many years. He remarked that it never had been necessary for him to shave oftener than every other day, or even at longer intervals. In cases 2 and 5 there was a frank appearance of dystrophia adiposogenitalis. In 7 of the 11 cases there was evidence of pituitary dysfunction of notable degree. A constant observation was the low systolic blood pressure; the highest value was 110 mm. of mercury, and in 6 of the 11 cases the value for the systolic blood pressure was 90 mm. of mercury or less.

Visual disturbances, in our experience, constituted the most common initial symptom; they were present in some form in every case. Progressive dimness of vision was the most common mode of onset, and in most instances (8 of 11 cases) this was the result of gradually developing primary atrophy of the optic nerve. It is noteworthy that in 6 of these 8 cases the defect in the visual field was bitemporal. Homonymous hemianopia (fig. 4) occurred in 4 cases; in 2 there was associated mild papilledema and in 1 there was a well advanced degree of primary atrophy of the optic nerve. A high degree of choked disk (4 diopters) was noted in only 1 case, the patient being a girl aged 5 years. Because of the age of the child the visual fields could not be outlined. In 1 case (case 2) there was a history of definite visual

21. (*a*) Frazier, C. H.: Pituitary Cachexia, Arch. Neurol. & Psychiat. **21**: 1-18 (Jan.) 1929. (*b*) Worster-Drought, C.; Dickson, W. E. C., and Archer, B. W. C.: Dyspituitarism of the Lorain Type, Associated with a Pituitary Cyst Arising from Rathke's Cleft and Secondary Lesions in the Hypothalamic Region and Ventricles, Brain **50**:704-718 (Oct.) 1927. (*c*) Warthin, A. S.: A Study of the Lipin Content of the Liver in Two Cases of Dyspituitarism, J. Lab. & Clin. Med. **2**:73-93 (Nov.) 1916. (*d*) Peet, M. M.: Pituitary Adamantinomas: Report of Three Cases, Arch. Surg. **15**:829-854 (Dec.) 1927.

22. Beckmann, J. W., and Kubie, L. S.: A Clinical Study of Twenty-One Cases of Tumour of Hypophyseal Stalk, Brain **52**:127-170 (July) 1929. Bartels.[11] Frazier.[21a]

hallucinations which had been associated with uncinate attacks. Four of our 11 patients had had periods of diplopia as a result of weakness of a cranial nerve. On theoretic grounds one would expect that the visual findings would indicate the situation of the lesion with reference to the optic chiasm, as well as shed some light on the probable anlage of the tumor. Many authors have discussed at length the reason for the great variation in the results of visual examination, including ophthalmoscopic study and examination of the visual field. It has been postulated that a tumor arising from the superior cell rests produces choked disks and secondary atrophy of the optic nerve, whereas one arising from the inferior cell rests causes early, primary atrophy of the optic nerve. Without doubt this is true in many instances. However, the surgical

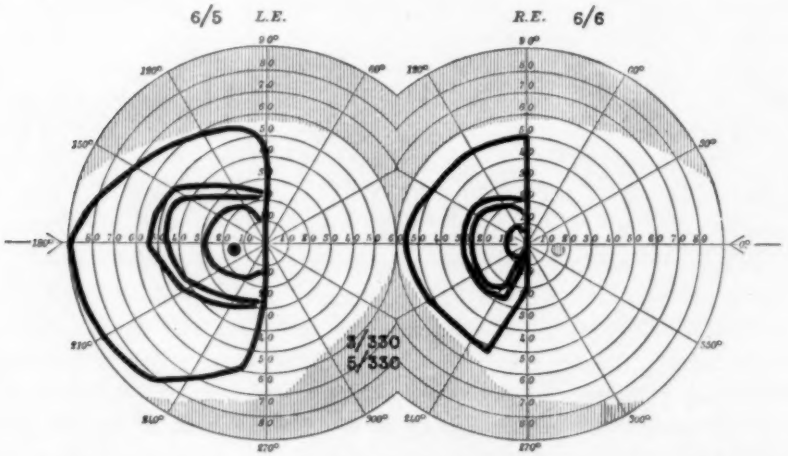

Fig. 4.—Preoperative visual fields in case 6, showing complete right homonymous hemianopia.

findings are generally such that accurate investigation of the probable origin of the tumor is not possible. No doubt many of the variations in the visual findings can be traced further to the normal anatomic variations which occur in the position of the optic chiasm, such as variations in the outline of the sella turcica, the pituitary body and the infundibulum. The frequency with which primary atrophy of the optic nerve was associated with a bitemporal defect in the visual field is interesting and perhaps significant; it no doubt signifies a prechiasmal situation of the lesion.

Many authors have reported that hypothalamic symptoms occupy a conspicuous place in the syndrome presented by this type of tumor. However, in our series they were neither prominent nor important. Polydipsia and polyuria were not observed. Drowsiness, although

evident in 5 cases, always appeared as a very late development and was probably secondary to the hydrocephalus rather than the result of primary involvement of the midbrain by the tumor.

Hydrocephalus was a prominent feature, although the symptoms of increased intracranial pressure, that is, headache and vomiting, generally appeared late in the course of the illness. Choked disk was definite in all 3 cases in which there was no primary atrophy of the optic nerve, and in all probability choked disk would have been present in all cases had not the atrophy preceded the increase of intracranial pressure. It is doubtful whether papilledema ever develops subsequent to the appearance of primary atrophy of the optic nerve. Headache was outstanding at some stage in 10 of the 11 cases and vomiting was present in 5 cases.

DIAGNOSIS

This type of tumor occurs predominantly in children or young adults, but doubtless it may remain small and asymptomatic for many years. In 5 cases symptoms had appeared before the patient was 10 years old, but in most instances several years had elapsed before the patients presented themselves for treatment. The oldest patient was a man aged 52, who had had a progressive loss of vision for four years (case 9).

The result of neurologic examination was, as a rule, essentially negative from an objective standpoint. In 4 cases there was definite mental disturbance, which consisted chiefly of lack of cooperation and failing memory. In case 11 the patient was so disturbed mentally that one physician had considered him psychotic. In 2 cases there was a clear history of recurrent olfactory hallucinations. The systolic blood pressure was uniformly low in each case.

Roentgenograms of the head disclosed positive evidence of bony erosion of the sella turcica in 10 of the 11 cases (fig. 1); contrary to many reports, this was the most constant single positive finding. Suprasellar calcification of varying degree was evident in 8 of the 11 cases; this percentage of cases is similar to that usually reported by other authors.[23]

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23. Camp, J. D.: Intracranial Calcification and Its Roentgenologic Significance, Am. J. Roentgenol. **23**:615-624 (June) 1930. Cushing, H.: The Intracranial Tumors of Preadolescence, Am. J. Dis. Child. **33**:551-584 (April) 1927. Dandy, W. E.: Brain Tumors: General Diagnosis and Treatment, in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1932, pp. 443-674. Luger, A.: Zur Kenntnis der im Röntgenbild sichtbaren Hirntumoren mit besonderer Berücksichtigung der Hypophysengangsgeschwülste, Fortschr. a. d. Geb. d. Röntgenstrahlen **21**:605-614, 1914.

DIFFERENTIAL DIAGNOSIS

In the absence of definite suprasellar calcification, patients who have visual disturbances and erosion of the sella turcica, with or without evidence of increased intracranial pressure, may present a very difficult problem in preoperative diagnosis. Although the age of the patient and the symptom complex may strongly suggest the presence of a tumor of the hypophysial duct, there are other lesions which may produce similar evidence of chiasmal or prechiasmal involvement.

Adenoma of the pituitary body produces a characteristic balloon-like enlargement of the sella turcica, bitemporal hemianopia and varying degrees of pituitary dysfunction. Meningioma generally occurs later in life than does tumor of the hypophysial duct; it often is associated with local osseous proliferation and an increased local vascularity of the skull. Primary tumor of the optic nerves or optic chiasm [24] generally causes a more rapid visual loss, which is often associated with an enlargement of the optic foramens. A vascular lesion in the region of the chiasm, such as an aneurysm of the circle of Willis or of the internal carotid artery, may produce visual disturbances and local erosion of bone. Bizarre lesions of the midbrain must be considered, as well as local inflammatory reactions that produce chronic chiasmal arachnoiditis.[25] A tumor of the brain remote from the optic chiasm may at times closely simulate a primary involvement of this region. Obstructive hydrocephalus associated with dilatation of the third ventricle often produces chiasmal signs and secondary erosion of the sella turcica.[26]

TREATMENT

Medical measures have no place in the treatment of a tumor of the hypophysial duct. They afford only temporary symptomatic relief. Palliation results only in more serious loss of vision or in gradual increase in the intracranial pressure. This type of tumor as Cushing [10] has stated, presents the most difficult problem in neurosurgery.

Radical surgical removal of the tumor offers the patient his only ray of hope, but this procedure is rendered exceedingly difficult by the relatively inaccessible situation of the lesion. The growth is surrounded at its base by vital structures which cannot be sacrificed and which will tolerate little, if any, traction or manipulation. Anteriorly are the optic nerves, laterally are the carotid arteries and posteriorly is the brain stem.

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24. Love, J. G., and Kernohan, J. W.: A Ganglioneuroma of the Optic Chiasm, Proc. Staff Meet., Mayo Clin. **12**:300-304 (May 12) 1937.

25. Craig, W. M., and Lillie, W. I.: Chiasmal Syndrome Produced by Chronic Local Arachnoiditis: Report of Eight Cases, Arch. Ophth. **5**:558-574 (April) 1931.

26. Bailey, P.: Concerning the Cerebellar Symptoms Produced by Suprasellar Tumors, Arch. Neurol. & Psychiat. **11**:137-150 (Feb.) 1924.

The circle of Willis completely surrounds the base of the tumor and thus adds materially to the difficulty of the surgical treatment.

As a rule the tumor has reached a considerable size by the time the patient presents himself for surgical treatment. Consequently, one is generally confronted with the problem of removal of a growth which has involved the third ventricle, has distorted and compressed the midbrain and has become intricately entwined in the diffuse arterial network at the base of the brain. Simple aspiration of the cystic portion of the tumor will naturally relieve the pressure, but such a procedure alone is of little value, as the cavity rapidly refills and the symptoms return. The most satisfactory surgical management consists in aspiration and collapse of the cyst, followed by as nearly complete a removal of the capsule as is anatomically possible.

In the pioneer days of neurosurgery the transsphenoidal approach was the accepted method of dealing with a lesion in the region of the optic chiasm. Although this method allowed access to the sella turcica, it was extremely unsatisfactory in an attempt to remove a lesion in which there had been suprasellar extension. In addition to the obvious anatomic limitations of this approach, there was always extreme risk of infection from the nasal cavity. Indeed, death from postoperative meningitis was fairly common when this method was in vogue.

Within the past ten years the intracranial transfrontal operation has completely supplanted the transsphenoidal method. With the advent of this approach the operative mortality and ultimate results have evidenced a decided improvement.[27] There is no longer the constant threat of postoperative infection, provided strict surgical asepsis is observed. The improved visualization of the entire anterior fossa of the cranium permits more accurate and extensive dissection and mobilization of the tumor.

The question of the side on which the transfrontal craniotomy is to be performed is generally decided on the basis of visual acuity. Experience has shown that the most satisfactory results are obtained in cases in which surgical removal is carried out on the side corresponding to the eye which shows the more marked visual loss. However, in cases in which the diminution of vision is equal bilaterally the operation of choice is a transfrontal craniotomy on the right, in view of the slighter postoperative reaction which follows manipulation of the right frontal lobe of the brain.

Craniotomy is performed through an anterior midline incision carried as far posterior as the coronal suture and then curved laterally to

27. Adson, A. W.: Operability of Brain Tumors, Ann. Surg. **100**:241-265 (Aug.) 1934; The Surgical Consideration of Brain Tumors, Northwestern Univ. Bull., Med. School **35**:1-42 (Dec. 31) 1934.

end in the posterior inferior temporal region (fig. 5). The skin and bone flaps are reflected separately. The anterior limb of the latter must be parallel to the supraorbital ridge and sufficiently far anterior to allow easy access to the floor of the anterior fossa. The approach to the optic chiasm may be made on either side of the dura mater and under the frontal lobe of the brain. The extradural method is preferable, but on occasion exposure may be improved by incising the dura over the frontal lobe and proceeding intradurally. The extradural approach becomes intradural at the lesser wing of the sphenoid bone.

In the presence of internal hydrocephalus, evacuation of the lateral ventricle by tapping of the anterior horn usually will afford adequate room beneath the frontal lobe by partially collapsing the hemisphere.

Fig. 5.—Postoperative photograph of a patient (case 7), showing the type of scalp incision employed in operation for a tumor in the region of the optic chiasm.

Prior to the introduction of intratracheal anesthesia it often was necessary to administer a hypertonic solution of dextrose intravenously to shrink the hemisphere and facilitate exposure of a tumor in the chiasmal region. In the absence of generalized increased intracranial pressure, adequate exposure is obtained relatively easily when intratracheal ether anesthesia is used.

The intratracheal tube suggested by Magill provides an adequate and free airway. This eliminates straining and difficult respiration, which produces venous engorgement with resultant increase in the intracranial tension, which in turn makes adequate exposure impossible without exertion of extreme traction on the frontal lobe of the brain. Aspiration of the cystic portion of the tumor is generally followed by collapse of the growth, which greatly reduces the tension within the

anterior fossa. In favorable cases collapse of the cystic portion affords sufficient exposure for gradual (piecemeal) removal of the tumor. Extreme care must be exercised at this point to avoid injury to the circulus arteriosus and the anterior cerebral arteries, which may be embedded in the tumor. It is inadvisable to attempt to remove the growth intact, as this is usually impossible without irreparable injury of the adjacent structures.

Careful, gentle handling of the tissues cannot be overemphasized in this as in all neurosurgical procedures. Well timed blood transfusions, we feel, are of inestimable value in such a case. Blood administered at the time the anterior fossa is being explored, prior to removal of the tumor, appears to reduce greatly the degree of surgical shock, as well as to supply the patient with some unknown factors which greatly aid his subsequent convalescence. The specific value of routine blood transfusion during the removal of such a tumor cannot, of course, be accurately estimated. Nevertheless, experience has shown that there is definitely more than a casual relation, and it is believed that routine transfusion in these cases will be followed by improved surgical results. Seven of our patients received transfusion (indirect sodium citrate method) on the operating table, although the blood was not needed to combat shock. One patient was given transfusion the day after the operation because of persistently low blood pressure. The question of drainage of craniotomy wounds is subject to much debate. Without entering a long discussion, we should like to say that it is our feeling that drainage of the wound for a period of twenty-four to forty-eight hours is of distinct value. Drainage was employed in every case in this series. Usually two Penrose cigaret drains are employed. One is placed under the frontal lobe, which has been elevated in order to facilitate removal of the tumor. This drain is extradural and does not come in contact with the optic nerves or the cortex cerebri. The other drain is left between the musculo-osseous flap and the scalp. The external ends of the drains are brought out through the posterior limb of the wound. Rarely, the first drain is brought straight out through a stab wound in the anterior temporal region.

In operations on children, among whom tumor of the hypophysial duct is most often seen, the time factor is worthy of careful consideration. We hesitate to discuss this point because, after all, accurate diagnosis, extreme consciousness of aseptic precautions and carefully planned and executed surgical technic, combined with well administered anesthesia, are the principal determinants of a successful outcome. However, craniotomy is a notoriously long procedure, and if it can be shortened without sacrifice of accurate hemostasis and safety this will be a boon to the surgeon and probably contribute to a lowering of mortality.

During the past year and a half, in the hospital service of one of us (J. G. L.) it has been customary to close the muscle, the temporal fascia and the galea aponeurotica of the supratentorial craniotomy wounds in operations performed for benign lesions with continuous catgut sutures instead of interrupted sutures of silk as was previously done. This saves a great deal of time and, so far as can be determined, has not caused any untoward developments in the healing of the wounds.

The average time required for the performance of each of these 11 reported operations was three hours and five minutes. The longest operation required four hours and fifteen minutes, and the shortest, one hour and forty-five minutes.

Postoperative care of the patient, which should include timely lumbar punctures for drainage and administration of pituitary preparations in case of water imbalance, is very important, tending to reduce morbidity and possibly mortality.

After the removal of the Penrose cigaret drains (twenty-four to forty-eight hours after the operation), if the patient complains of headache or has fever or stiffness of the neck a lumbar puncture is performed while the patient is in the horizontal position on his side, with the craniotomy wound uppermost to avoid pressure and discomfort. The pressure of the cerebrospinal fluid is determined with an Ayer manometer, and the pressure is reduced slowly to half of the original value. If the fluid is bloody or xanthochromic, spinal punctures should be performed daily until the fluid is clear. Two or three punctures usually are sufficient.

If the water balance is negative, that is, if the urinary output is greater than the total fluid intake, posterior pituitary should be administered. Usually, 0.5 cc. of a solution of posterior pituitary administered hypodermically twice daily will correct the fluid discrepancy and relieve the thirst which is a usual accompaniment. A few days of this therapy will usually suffice. If the imbalance should recur, nasal insufflation of powdered posterior pituitary is a better method of treatment. The patient can administer this preparation in this manner without aid and without a hypodermic syringe.

REPORT OF CASES

CASE 1.—A girl aged 5 years was brought to the clinic April 15, 1935, because of progressive impairment of vision. She had been well until one year prior to her registration, when the parents noted that her vision was not normal and that her right eye turned outward. She never had headache or nausea, and she had not vomited. The values for the systolic and diastolic blood pressure were 88 and 58 mm. of mercury, respectively, and the pulse rate was 92. The results of general examination were essentially negative.

Ophthalmologic examination revealed only light perception in the right eye and the ability to count fingers at 10 feet (3 meters) with the left eye. There

was temporal hemianopia in the left eye, and there was only a residual temporal field in the right eye. Funduscopic examination disclosed evidence of bilateral atrophy of the optic nerve. There was convergent strabismus of the right eye. The pupils and reflexes were normal.

Roentgenograms of the head revealed a calcified tumor 5 cm. in diameter just above and anterior to the sella turcica; calcification had occurred in the walls of the tumor. There was evidence of secondary erosion of the sella turcica and thinning of the floor of the anterior fossa on the left side. Neurologic examination disclosed no abnormality. A diagnosis of suprasellar cyst was made. A transfrontal craniotomy on the right side was performed, intratracheal ether anesthesia being used. The anterior horn of the right lateral ventricle was tapped; this allowed the brain to collapse and permitted excellent exposure. A very large cystic tumor was found; its position was both intrasellar and extrasellar. Both optic nerves were displaced laterally and were stretched to several times their normal length. Aspiration of 4 ounces (120 cc.) of thick, dark yellow fluid collapsed the cyst, which was then incised, and a large amount of grumous material was removed. The cyst was removed, and the third ventricle was opened. The wound was closed in the usual anatomic manner. One Penrose drain was left adjacent to the sella turcica, and one was left between the scalp and the bone flap. The microscopic diagnosis was tumor of the hypophysial duct. Convalescence was entirely uneventful. The patient was dismissed on the fifteenth postoperative day. The results of another neurologic examination, which was made before the patient was dismissed, were essentially negative. It was observed that the strabismus had entirely disappeared. Visual acuity at the time of the patient's dismissal was approximately the same as at the time of the original examination.

Comment.—This case illustrates the tragic result of postponing surgical intervention when pressure on the optic nerves has developed. It further emphasizes the irreparable atrophy of the optic nerve which results from long-continued local pressure.

Case 2.—A man aged 26 was referred to the clinic in July 1935 because of headaches and an endocrine disturbance. He said that he was well until the age of 9 years; however, at the age of 6 or 7 years he had severe headaches, which occurred periodically for two years. He stopped growing at the age of 9 years. He did well in school until his junior year in high school, when he failed in several courses and found it difficult to concentrate. His voice did not change. Between the ages of 21 and 26 his height increased 4 inches (10 cm.). Two years prior to his admission to the clinic he noted decreased vision in the left eye; decrease progressed gradually. The nasal field in the left eye was the last to lose its vision, and for a year before the patient came to the clinic he was completely blind in the left eye. A short time before he came to the clinic he noted that he bumped into objects to his right unless he turned his head. Periodic peculiar odors and visual hallucinations associated with olfactory hallucinations were noticed three or four times a week during the year prior to his admission. Generally, he felt well except for tiredness and drowsiness, which had been noted a short time before he came to the clinic.

The results of general physical examination were essentially negative. The values for the systolic and diastolic blood pressure were 84 and 62 mm. of mercury, respectively, and the pulse rate was 72. The patient's features were those of a boy of 11 or 12. Endocrine dysfunction was evidenced by the absence of body hair and by the narrrow shoulders, broad hips, pads of fat over the pubes and trochanters, short trunk, long, slender arms and long, tapering fingers.

The face was smooth and beardless. The skin appeared soft, white and smooth. The voice was high pitched. The prostate gland was rudimentary, and the genitalia were infantile. Ophthalmologic examination disclosed amaurosis in the left eye and 6/5 vision in the right eye. There was temporal hemianopia in the right eye, and marked primary atrophy of the optic nerve was present in the left eye. Roentgenograms of the head revealed enlargement, grade 3, of the sellae turcica and destruction of its floor. The posterior clinoid processes and the dorsum sellae were eroded. Neurologic examination revealed moderate generalized weakness of the arms and legs. The deep tendon reflexes were diminished or absent, even on reenforcement. The Babinski phenomenon was present on the right side. The direct light reflex was absent in the left eye. The diagnosis was tumor of the pituitary body.

With the patient under intratracheal ether anesthesia, a transfrontal craniotomy was performed on the left. The brain was tense, and the dura bled freely. An attempt to tap the left anterior horn was unsuccessful. Careful elevation of the left frontal lobe disclosed a large cystic tumor which filled the sella turcica and displaced the optic chiasm posteriorly. The left optic nerve was flattened, and only a small part of its substance remained. The right optic nerve was less involved but was much smaller than usual and appeared concave on the mesial aspect as a result of local pressure. The capsule of the tumor was opened, and a large amount of dark brown grumous material, which contained crystals of cholesterol, escaped. Very little solid tissue was present in the tumor. A subtotal removal of the capsule was easily effected without trauma to the adjacent structures. A Penrose cigaret drain was placed beneath the frontal lobe, and another was placed between the skin and the bone flap.

The convalescence was uneventful. Another neurologic examination, made before the patient left the clinic, revealed essentially the same findings as were obtained before operation; this was also true of examination of the ocular fundi and visual fields, except that light perception was present in the left eye and subjective visual improvement was noted in the right eye. The pathologist made a diagnosis of tumor of the hypophysial duct.

Case 3.—A man aged 31 was admitted to the clinic on Dec. 12, 1935, because of progressive impairment of vision. He always had been nervous, shy and slightly backward. He stuttered until he was of high school age. Six months before his registration at the clinic he had "the flu," which lasted about one week. Soon thereafter he first noted that the vision in the right eye was not normal. Photophobia and further impairment of sight developed, as well as a "blind spot" in the right eye. Dull frontal headaches began about this time. They occurred two or three times a week and were worse in the evening. There were also periodic sharp pains in the frontal region. The headache was intensified by stooping, jarring and straining. Three months before he came to the clinic vomiting occurred, associated with nausea. The vomiting occurred intermittently and was worse when he became nervous or when he suddenly assumed an erect posture.

The patient was pale. The values for the systolic and diastolic blood pressure were 110 and 82 mm. of mercury, respectively, and the pulse rate was 74. There was a feminine distribution of pubic hair. Ophthalmologic examination revealed visual acuity to be 6/10 in the left eye, and the patient was able to count fingers with the right eye. Examination of the visual fields revealed bitemporal hemianopia (relative), a central scotoma in the right eye and enlarged blindspots in both eyes. Funduscopic examination disclosed a suggestive pallor in the left eye and in the temporal portion of the right optic disk. The diagnosis was

chiasmal lesion, more prechiasmal on the right than on the left. Roentgenograms of the head disclosed enlargement, grade 3, of the sella turcica; there also was evidence of erosion of the floor of the sella turcica and of the posterior clinoid processes. There was slight calcification at the outlet of the sella turcica. The diagnosis was chiasmal lesion.

With the patient under intratracheal ether anesthesia, a transfrontal craniotomy was performed on the right. The right optic nerve was swollen and had been displaced mesially and upward by a reddish purple mass which was situated between the nerve and the right ophthalmic artery, which was displaced laterally. The left optic nerve appeared normal. The tumor appeared to have arisen from within the sella turcica, but it extended beyond the confines of that structure. The cystic mass was aspirated, and yellow fluid was obtained. The capsule was split, and a large quantity of gray grumous material was aspirated through a brain cannula. A portion of the capsule was resected. Cholesterol crystals were clearly visible floating on the physiologic solution of sodium chloride while the the anterior fossa was being irrigated. The wound was closed in the usual anatomic manner; one Penrose cigaret drain was left in the anterior fossa. Convalescence was uneventful. The patient was dismissed from the hospital on the twelfth postoperative day. Microscopic examination revealed a typical tumor of the hypophysial duct. A neurologic examination made before the patient left the clinic did not reveal any abnormality. Ophthalmologic examination disclosed improvement in vision, which was 6/7 in the left eye and 6/12 in the right eye. The pallor of the optic disk remained the same as prior to operation. Examination of the visual fields revealed a questionable homonymous defect on the left, which had become much fuller in extent.

Case 4.—A boy aged 5 years was brought to the clinic on April 27, 1936, because of headaches, vomiting and diplopia. About four months prior to his registration the patient began to complain of headaches, which usually were worse in the morning. At the time he was brought to the clinic they had become more frequent and more severe. About three weeks prior to his examination it was noticed that his left eye "turned in." At times he became very drowsy. This drowsiness would persist for several days and then disappear. There was constipation for two or three months prior to his admission to the clinic. The values for the systolic and diastolic blood pressure were 82 mm. and 60 mm. of mercury, respectively. The pulse rate was 76, and the temperature was 99.6 F. A definite cracked pot note was elicited by percussion of the head. Ophthalmologic examination disclosed papilledema of 4 diopters on the right side and 3 diopters on the left side. There were no hemorrhages. On account of the age of the patient and the lack of cooperation, the visual fields were not determined. Roentgenograms of the head revealed increased intracranial pressure, enlargement of the sella turcica, erosion of its floor and of the posterior clinoid processes and small areas of calcification within and just above the sella turcica. Neurologic examination did not disclose any abnormality. The diagnosis was cyst of Rathke's pouch.

On May 2, 1937, with the patient under ether anesthesia, a transfrontal craniotomy was performed on the right. The contents of a suprasellar and intrasellar cyst were removed, and the wall of the cyst was resected. Because of increased intracranial pressure it was necessary to tap the anterior horn of the right lateral ventricle and evacuate a large quantity of cerebrospinal fluid before the right frontal lobe could be elevated sufficiently to permit exploration of the region of the sella turcica. When the frontal lobe had been elevated and

the dura mater incised along the wing of the sphenoid bone, the right optic nerve was easily exposed. To the left of this nerve there was a large, blue thin-walled cyst. The wall of the cyst contained calcium. The cyst was opened, and 20 cc. of greenish yellow fluid which contained cholesterol crystals and a large quantity of calcium was obtained. When the cyst had been collapsed, the anatomic structures about the sella turcica were identified, and it was noted that the bulk of the cyst was situated on the left of the left optic nerve, the optic chiasm and the left internal carotid artery. The optic chiasm was ballooned out and appeared cystic. The chiasm was not incised, as it was felt that the apparent cystic change in this structure might well be the result of edema secondary to stasis caused by local pressure by the tumor. The wall of the tumor was gradually coagulated by means of the electrosurgical unit and was partially resected. When the tumor had been removed, the optic nerves and optic chiasm appeared to have been decompressed completely. A Penrose cigaret drain was left under the right frontal lobe and brought out through the posterior limb of the craniotomy incision. The patient's convalescence was satisfactory, and the wound healed by primary intention. Microscopic examination of the tissue removed at operation revealed the characteristic appearance of a tumor of the hypophysial duct. Postoperative neurologic examination did not reveal any change in the preoperative condition; ophthalmologic examination disclosed receding papilledema and some secondary atrophy of the left optic nerve.

This patient recently underwent another craniotomy elsewhere, because of a recurrence of the symptoms.

CASE 5.—A youth aged 18 registered at the clinic on Oct. 9, 1936, because of headaches, vomiting and impairment of memory. The first attack of headache occurred in 1931. This attack was associated with vomiting, which lasted six to eight hours. The attack was followed by exhaustion. The second attack occurred in 1932; this was followed by similar ones in 1933 and 1934. Each succeeding attack was more severe and lasted longer than the previous one. The patient said that his general health between attacks was good. In 1935 his lack of physical development was noted, and a diagnosis of dystrophia adiposogenitalis was made. He was given thyroid extract, and later high voltage roentgen therapy was applied to the sellar region. After the roentgen therapy he became very ill for three weeks; severe headache, vomiting and malaise were present. Two months before he came to the clinic, administration of solution of posterior pituitary produced marked improvement. He did not vomit while this preparation was being administered. However, the headache was not relieved. During the few months prior to his admission to the clinic the patient became more drowsy, his memory became very poor, and vomiting not only reappeared but became projectile. The patient was underdeveloped for his age; he had the stature of a child of 12 years. He had a feminine type of deposition of fat and lacked secondary sexual characteristics. The values for the systolic and diastolic blood pressure were 94 and 66 mm. of mercury, respectively. The pulse rate was 68. There was a waxy pallor; the skin was dry but soft. A bruit was heard in both temporal areas. Ophthalmologic examination disclosed 6/10 vision in the right eye and the ability to see moving objects with the left eye. Examination of the visual fields revealed bitemporal hemianopia (residual nasal field). Examination of the ocular fundi disclosed moderate temporal pallor of the right optic disk and generalized pallor, grade 3, of the left optic disk. Roentgenograms of the head revealed diffuse calcification in the midline at the outlet of the sella turcica and some destruction of the dorsum sellae (fig. 1). The diagnosis was tumor of the hypophysial duct.

On Oct. 20, 1936, with the patient under ether anesthesia, a transfrontal craniotomy was performed on the left. The ether was administered through an intratracheal tube. The frontal lobe was tense, and the brain was elevated with considerable difficulty. Numerous adhesions were present between the brain and the underlying tumor. A characteristic thin-walled cyst, which contained calcium, was found. Aspiration of the cyst produced approximately 20 cc. of brownish fluid, which contained crystals of cholesterol. The portion of the cystic wall which could be easily mobilized after collapse of the cyst was carefully resected. There had been compression of the optic nerves and, although the greatest visual loss was on the left side, the left optic nerve appeared larger and more nearly normal than the right. The wound was closed in the usual anatomic manner; two Penrose cigaret drains were inserted as a precautionary measure. The microscopic diagnosis was tumor of the hypophysial duct. The wound healed by primary intention, and the convalescence was uneventful except for a period between the third and the sixth postoperative days, when spinal puncture was done on two occasions to relieve a moderate degree of increased intracranial pressure. The convalescence thereafter was satisfactory. The patient was dismissed from the hospital on the twelfth postoperative day, at which time his condition was

Fig. 6—Postoperative photograph of the patient in case 5; the picture was taken two weeks after the operation.

excellent and his vision much improved (fig. 6). He was able to recognize gross objects with his left eye. A recent report stated that his general health was excellent, that his vision was very good, that he could read well with either eye and that he had had no headaches since he left the clinic.

CASE 6.—A man aged 33 registered at the clinic May 25, 1936, because of headaches which had occurred for one year. He had had frontal headaches as far back as he could remember, but these had not been as severe as the headaches which occurred during the year before he came to the clinic. The latter were bilateral frontal headaches; at times the pain extended to the occipital region. The headaches occurred daily and were of increasing severity. For about one month prior to registration the attacks were periodic and characterized by an aura. During these attacks he felt as if he were going to lose consciousness. The attacks were followed by a peculiar odor which "smelled like medicine." These uncinate attacks lasted about a minute and were followed by an increase of pain in the head. They occasionally awakened him at night. He often had as many as three or four attacks during the day, and at times he had to leave his work and lie down. The patient felt that his memory for recent events was failing. Because of blurring of vision he consulted his local physician, who prescribed glasses. These produced temporary relief. There was a loss of the sense of

smell on the left side. The results of general physical examination were essentially negative. The values for the systolic and diastolic blood pressure were 111 and 80 mm. of mercury, respectively. The pulse rate was 72. Ophthalmic examination disclosed that vision was 6/6 in the right eye and 6/5 in the left eye. Examination of the ocular fundi disclosed blurring about the nasal margins of both optic disks and moderate venous congestion. The arteries and veins were dilated; this suggested early edema of the optic disk. However, there was no measurable elevation of the optic disks. Perimetry disclosed complete right homonymous hemianopia (fig. 4). Roentgenograms of the head disclosed an irregularly calcified shadow, which was situated within and extended above the sella turcica. There also was evidence of secondary erosion of the floor of the sella turcica, of the posterior clinoid processes and of the dorsum sellae.

On June 4 a transfrontal craniotomy was performed on the right. The brain was under definitely increased pressure, and it was with difficulty that the right frontal lobe was elevated sufficiently to expose the large, thin-walled cystic tumor

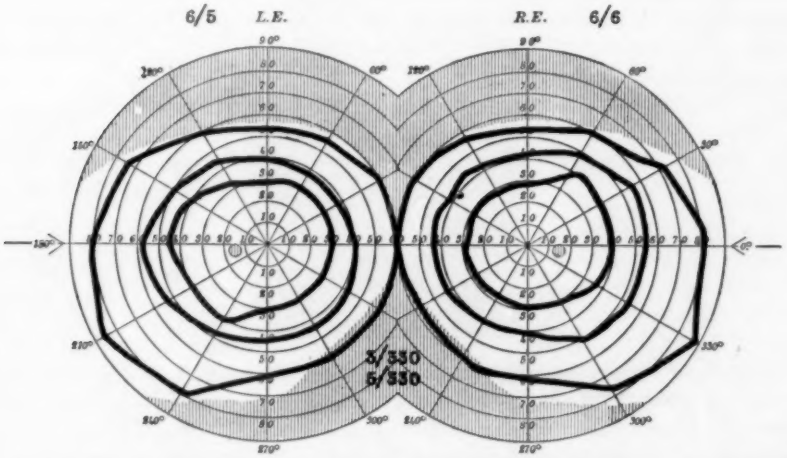

Fig. 7.—Normal fields of vision with normal central vision after removal of a tumor of the hypophysial duct (case 6).

which was situated to the left of the optic chiasm and the left optic nerve and which had displaced these structures to the right. The thin wall of the cyst contained a large quantity of calcium. Three ounces (90 cc.) of yellow fluid, which was loaded with cholesterol crystals, was obtained from the tumor. Aspiration collapsed the wall of the cyst and reduced the intracranial pressure sufficiently to permit excellent exposure of the structures about the sella turcica. The right optic nerve was about normal in length and was only slightly displaced. The left optic nerve, however, was definitely elongated and arched toward the right side. The capsule of the tumor was delivered beneath and around the left optic nerve and removed. A Penrose cigaret drain was left under the right frontal lobe and was brought out through the posterior limb of the craniotomy wound. Histologic examination disclosed a typical tumor of the hypophysial duct. The wound healed by primary intention, and the patient's convalescence was rapid. He was dismissed from our care on June 16; at this time he was free from headaches, and neurologic examination did not disclose any abnormality except the loss of the sense of smell.

There had been no recurrence of the uncinate attacks. Vision was normal, and the visual fields were normal (fig. 7). There was no edema of the optic disks.

CASE 7.—A boy aged 11 was brought to the clinic on Aug. 8, 1936, because of progressive loss of vision in both eyes. Three years prior to his admission, during a routine physical examination at school, a nurse noted defective vision in his right eye. The child, however, did not complain of poor vision until one year before he came to the clinic. One month before his admission, frontal headaches occurred daily for three weeks. They were moderately severe. From the time he was 18 months of age his nose bled frequently; the epistaxis was always worse in hot weather. During the month before his admission epistaxis occurred daily and often was preceded by headache, which was relieved after his nose had bled for a few minutes. The results of general physical examination were essentially negative. The values for the systolic and diastolic blood pressure were 96 and 62 mm. of mercury, respectively. The pulse rate was 78.

Ophthalmic examination revealed that vision was 6/10 in the left eye and 6/30 in the right eye. Relative bitemporal hemianopia and relative central scotoma of the right eye were disclosed. The optic disks appeared full nasally but were not definitely edematous. There was pallor, grade 1, of the temporal part of the right optic disk, but there was no definite pallor of the left optic disk. Roentgenograms of the head revealed enlargement of the sella turcica and slight thinning of its floor and of the posterior clinoid processes. Neurologic examination did not reveal any abnormality. There was no evidence of endocrine dysfunction, although the child was puny, pale and listless. The diagnosis was chiasmal lesion.

A transfrontal craniotomy was performed on the right, with the patient under intratracheal ether anesthesia. A large suprasellar and intrasellar thin-walled cyst was found; this was situated in front of the optic chiasm and had displaced both optic nerves laterally. Approximately 25 cc. of thick yellow fluid was removed, and a considerable proportion of the wall of the cyst was removed. The cyst contained a great deal of calcium. A portion of the capsule of the cyst, which was behind and under the optic chiasm, could not be removed, but both optic nerves were thoroughly decompressed. One Penrose cigaret drain and one Penrose drain were inserted, and the wound was closed in the usual anatomic manner. Convalescence was satisfactory, and the wound healed by primary intention (fig. 5). Histologic examination revealed a typical tumor of the hypophysial duct. Postoperative neurologic examination did not reveal any abnormality. Ophthalmic examination demonstrated great improvement in the vision. The vision in the left eye was 6/6, and that in the right eye was 6/30. No significant change had occurred in the ocular fundi since the previous examination. The visual fields showed marked improvement; that of the left eye was reported as normal, and there was only a suggestive temporal notch in the visual field of the right eye. However, the relative central scotoma remained unchanged. When the patient was last heard from his condition was satisfactory, and there had been no further loss of vision.

CASE 8.—A woman aged 25 came to the clinic on Nov. 25, 1936, because of headaches and amenorrhea. Until the age of 17, she menstruated regularly, at which time the menstrual periods began to be irregular. Amenorrhea for as long as three months occurred often. The menses gradually decreased in frequency and amount, and from the age of 20 on amenorrhea prevailed. Many types of glandular therapy were tried without avail. For several years prior to her admission to the clinic she had headaches which became more severe during the last six months. No visual trouble had been noted by the patient. For the past

few months drowsiness had been marked. The drowsiness was increasing. The patient fell asleep easily and frequently. Although her mentality had become slower than usual, she was able to continue her work as clerk in a store. Two days before she came to the clinic she had the first attack of vomiting, which began at 4 a. m. "Convulsions" occurred four times during the following day, and one "generalized" grand mal seizure was described by the home physician. Drowsiness increased. The results of general physical examination were essentially negative. The values for the systolic and diastolic blood pressure were 108 mm. and 75 mm. of mercury, respectively. The pulse rate was 58. Ophthalmic examination disclosed normal visual acuity. Examination of the visual fields disclosed homonymous hemianopia of the right lower quadrant. Funduscopic examination revealed edema of the nasal margins of both optic disks. The elevation was 1 to 2 diopters in the right eye and 2 diopters in the left eye. Hyperemia of both optic disks and venous engorgement also were present. There were several hemorrhages along the veins in the right eye at some distance from the optic disk. Several small punctate hemorrhages were present near the macula, and there also were some large, deep hemorrhages in the same region. Roentgenograms of the skull revealed diffuse particles of calcification, which extended backward and upward from the dorsum sellae, and destruction of the superior portion of the dorsum sellae. Neurologic examination revealed that the attention, cooperation and memory of the patient were much below normal. The patient was obese. She was unsteady on her feet and seemed to totter to the left. She had difficulty when she tried to stand on her right or left foot while her eyes were closed; this difficulty was more marked when she attempted to stand on her left foot. The diagnosis was tumor of the hypophysial duct.

In view of the right homonymous hemianopia, a left transfrontal craniotomy was performed on November 28, with the patient under intratracheal ether anesthesia. In spite of the choked disk the brain was not under great tension, and there was considerable fluid in the cisterna chiasmatica, which when removed allowed a satisfactory visualization of the optic chiasm. No tumor, however, could be seen. Elevation of the frontal lobes from the optic chiasm revealed a bluish tumor which was situated posterior to the chiasm, between the optic tracts. It was cystic and contained calcium in its walls. One ounce (30 cc.) of brownish fluid was aspirated, which allowed the cyst to collapse. Extensive resection of the capsule of the tumor was then effected, which thoroughly decompressed the optic tracts and chiasm. Two Penrose cigaret drains were inserted. Histologic examination revealed a typical tumor of the hypophysial duct.

Convalescence was stormy for the first few days, and there was weakness of the right arm and leg. There was gradual improvement in motor power. An acute elevation of temperature occurred on the sixth postoperative day but subsided immediately after aspiration of the flap and removal of several cubic centimeters of serum. At the time the patient was dismissed, on the twenty-second day, her condition was much improved. Neurologic examination did not reveal any abnormality except slight weakness on the right side, which was gradually improving. The vision was 6/6 in both eyes. The visual field appeared much improved, and the papilledema had entirely receded. When the patient was last heard from she was in good health, her appetite was excellent, and the weakness of the right side had decreased so that she was able to walk without a limp.

Comment.—This case illustrates the great diversity of symptoms associated with this type of tumor. Although menstrual irregularity was present for years, no other definite symptoms appeared until six months

before the patient came to the clinic. She had never noted any visual difficulty, although bilateral papilledema was present and there was definite homonymous hemianopia of the lower right quadrants. The optic fundi presented an appearance not usually associated with increased intracranial pressure, but it closely simulated that of retinitis septica, such as is commonly seen in cases of subacute bacterial endocarditis. Repeated cultures of the blood were sterile. The site of the tumor was rather unusual; it was posterior to the optic chiasm and was situated between the optic tracts.

CASE 9.—A man aged 52 registered at the clinic Jan. 11, 1937, complaining of progressive loss of vision.

Four years before the patient came to the clinic he discovered a loss of vision in the temporal half of the left eye. New glasses did not produce much relief. Six months later he noted that vision in the temporal field of the right eye was failing, and thereafter there was gradual but steady loss of vision except for one short period early in his illness, when the vision first in the left and then in the right eye seemed to improve definitely for a few weeks. During the six months prior to his registration at the clinic the patient noticed diplopia for close objects. The second image appeared just above the real image. Headaches were present for three years; they were dull and throbbing and were situated in the left occipital and cervical regions. They were periodic and lasted only one to six hours, beginning and ending abruptly.

The results of general physical examination were essentially negative. The values for the systolic and diastolic blood pressure were 110 and 76 mm. of mercury, respectively. The pulse rate was 84. Ophthalmic examination revealed that the vision in the left eye was 6/30; a bitemporal visual defect and a central scotoma were present in the left eye. Examination of the ocular fundi revealed pallor, grade 2, of the right optic disk; there was no visible loss of substance. There was pallor, grade 3, of the left optic disk; there also was a loss of substance in the temporal portion of the left disk. Urinalysis disclosed no abnormality. The concentration of hemoglobin was 15.4 mg. per hundred cubic centimeters of blood. There were 4,500,000 erythrocytes and 7,500 leukocytes in each cubic millimeter of blood. The flocculation test for syphilis gave negative results. Roentgenograms of the head did not disclose any abnormality. Roentgenograms of the optic canal revealed that the right optic foramen was larger than the left; this probably was the result of an anatomic variation. Neurologic examination revealed no abnormality; the cerebrospinal fluid was normal. A diagnosis of chiasmal lesion was made.

A left transfrontal craniotomy was performed with the patient under intratracheal ether anesthesia. A large, thin-walled cystic tumor was situated anterior to the optic chiasm. There were extensive adhesions between the tumor and both optic nerves. The cyst was aspirated, and 20 cc. of dark, dirty greenish material was removed. The capsule of the cyst was resected. A considerable amount of grumous material and flecks which resembled cholesterol crystals were found, chiefly in the portion beneath the left optic nerve. Both optic nerves and the optic chiasm were thoroughly decompressed. The optic nerves appeared definitely smaller and paler than normal. Two Penrose cigaret drains were inserted, and the wound was closed in the usual anatomic manner. Microscopic examination revealed a typical tumor of the hypophysial duct. The convalescence was uneventful except for a few episodes of acute hypopituitarism, which were

evidenced by low blood pressure and increased urinary output. These symptoms were controlled by hypodermic injections of a solution of posterior pituitary; they later were controlled by nasal insufflation of posterior pituitary. The patient was dismissed from the hospital two weeks after the operation. At that time the neurologic examination did not reveal any abnormality. The vision, which had improved, was reported as 6/7 in the right eye. Considerable improvement was also noted in the visual field. Only light perception was present in the left eye. The pallor of the optic disk was essentially the same as it had been at the time of the preoperative examination. When last heard from, the patient said that he had noticed much visual improvement. It has been necessary for him to continue endocrine therapy because of mild hypopituitarism.

Comment.—In spite of the rather large lesion about the optic chiasm, there was no roentgenographic evidence of osseous change in the sella turcica. Definite evidence of osseous erosion is usually evident roentgenographically four or more years after the onset of symptoms, but for some unknown reason such evidence was not observed in this case.

The advanced age of the patient is unusual. This case illustrates the fact that a tumor anlage may lie dormant for many years and then, for some unexplainable reason, undergo cellular proliferation and form a tumor.

Case 10.—A girl aged 9 was brought to the clinic by her parents on Feb. 8, 1937, because of headaches, vomiting and an almost total loss of vision. For five or six years prior to this she had afebrile attacks of vomiting; these attacks were preceded by nausea. They occurred every four to six weeks and lasted one or two days. The attacks continued, but there was no progression in their severity. One year before the patient was brought to the clinic, it was observed that her vision was much impaired. The patient's mother also noted that the right eye frequently turned upward and outward. The patient complained frequently of double vision. Four months before she came to the clinic she began to have frontal headaches. Just prior to her registration drowsiness and somnolence were noted by the parents for the first time. General physical examination revealed a systolic blood pressure of 90 mm. of mercury and a diastolic pressure of 60 mm. of mercury. A cracked pot sound could be elicited over the left frontal and parietal regions of the skull. Ophthalmic examination revealed that vision was 6/30 in the left eye and that the patient could perceive only light with the right eye. Examination of the visual field disclosed temporal hemianopia and a depressed field in the left eye and a residual nasal field in the right eye. Funduscopic examination revealed evidence of atrophy of the optic nerve, which was more advanced in the right eye than in the left. Roentgenograms of the head disclosed evidence of increased intracranial pressure, extensive destruction of the sella turcica and erosion of the anterior and posterior clinoid processes. Neurologic examination disclosed no abnormality. The diagnosis was tumor of the hypophysial duct. Exploration was advised but not urged, in view of the grave surgical risk. The parents requested that operation be attempted in the hope of affording the child some degree of relief.

A transfrontal craniotomy was performed on the right with the patient under intratracheal ether anesthesia. A large, thick-walled cyst was exposed; it was situated between the optic nerves and had displaced the optic chiasm posteriorly. Thirty cubic centimeters of dark brown fluid was obtained by aspiration of the

cavity. The wall of the cyst was incised, and a large amount of thick coarse material, which contained calcium, was removed. Extensive resection of the capsule was carried out. The capsule was 1 cm. thick in the more posterior portion, which was situated beneath the optic chiasm; however, further anteriorly, it became very thin, in certain portions measuring less than 1 mm. in thickness. The optic nerves were unusually vascular. Two Penrose cigaret drains were inserted as a precautionary measure. The convalescence was uneventful. The results of another neurologic examination were essentially the same as those observed at the preoperative examination. There was subjective visual improvement in spite of the lack of objective evidence of improvement. The visual acuity was 4/6 in the left eye; only perception of light was present in the right eye. The patient returned to the clinic in four months because of attacks of excessive vomiting, which had occurred five or six times daily. Neurologic examination again failed to disclose any abnormality. Ophthalmic examination revealed a further reduction in vision.

CASE 11.—A boy aged 16 was brought to the clinic on Jan. 12, 1938, because of a distinct mental change. His illness began in the summer of 1937, when he had headaches in the frontal regions and over the vertex. In the fall of that year he complained of blurring of vision and diplopia when he was reading. At about the same time his grades, which formerly had been good, became very poor, and he failed to participate in the usual activities at school. On Jan. 8, 1938, he became very drowsy; he fell asleep at the table and slept all day and all night. He lost all interest in things about him, and his mental reactions were silly. He became facetious. His judgment became poor, and there was a complete change in his personality. He walked up to strangers and pulled their ties and pulled their pencils out of their pockets; he also did many acts with compulsion. His appetite became enormous, and he gained considerable weight. Likewise, there was an increase in thirst, with an increase in urinary output. His parents said that he drank a gallon of liquid a day and passed a corresponding quantity of urine.

His height was 5 feet 6½ inches (171.9 cm.) and his weight was 144 pounds (65.3 Kg.). The value for the systolic blood pressure was 100 mm. of mercury, and that for the diastolic pressure was 60 mm. The pulse rate was 48. During the examination the patient was noisy. He giggled and shouted without cause. Ophthalmic examination revealed that vision was 6/30 in the right eye and 3/60 in the left eye. The examination disclosed pallor, grade 2, of the right optic disk and pallor, grade 1, of the left optic disk. There were small areas of pigment degeneration in each macula. Examination of the visual field revealed a right homonymous hemianopia of an incongruous type. There was a central scotoma in the left eye. The neurologic examination did not disclose any abnormality. Roentgenograms of the head revealed an irregular mass of calcium, 2.5 by 3 cm., directly above the posterior clinoid processes. The tumor appeared to be in the midline, and there was some evidence of pressure erosion of the left posterior clinoid process. The roentgenographic evidence suggested that the tumor probably involved the third ventricle. An encephalogram disclosed evidence of a suprasellar tumor which occupied a position corresponding to the position of the calcium seen in the original roentgenograms. The third ventricle was displaced upward and backward by the tumor mass. In view of these findings the diagnosis was tumor of the hypophysial duct.

On January 20 a transfrontal craniotomy was performed on the left. This disclosed a large, thin-walled cystic tumor which was situated posterior to the optic chiasm. This made adequate exposure of the tumor difficult. The only

approach to the tumor was behind the optic chiasm and anterior to the anterior communicating artery. A hollow needle was inserted through the thin wall of the tumor, and about 20 cc. of yellow fluid was removed. This collapsed the cystic tumor and removed the abnormal pressure from the optic tracts and optic chiasm. Only a small portion of the capsule was resected, because of the inaccessible position of the tumor. Microscopic examination of the capsule of the tumor revealed a typical tumor of the hypophysial duct. The wound was closed in the usual manner after one Penrose cigaret drain had been inserted beneath the left frontal lobe and another between the scalp and bone flaps. During the operation a transfusion of 500 cc. of citrated blood was given. The patient's convalescence was characterized by intermittent fever. His temperature ranged from normal to 102 F. daily. However, his general condition seemed to be excellent, and he was mentally clear and alert. Another neurologic examination disclosed the same mental reactions as had been present prior to the operation. Postoperative ophthalmic examination revealed no change except a mild edema of the nasal portion of the left optic disk.

SUMMARY

Tumor of the hypophysial duct is extremely rare. Few articles on the subject have been published. It is hoped that the present report of a series of 11 consecutive cases in which operation was performed without a death will stimulate other physicians to take a more active interest in this condition and to make the diagnosis early, before irreparable injury has been caused by long-continued pressure on the visual pathways.

Although the presenting symptoms are usually those referable to the eyes, glasses and medical treatment are not beneficial in counteracting the pressure effects of an intracranial neoplasm. Transfrontal craniotomy with as extensive removal of the tumor as is consistent with good surgical judgment is the treatment of choice.

Organotherapy is useful and is indicated in some cases, but its role is secondary to that of removal of the tumor.

CONCEALED CHRONIC ALCOHOLISM IN SURGICAL PATIENTS

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It seems worth while to present some facts about surgical patients who may be said to be suffering from a condition I wish to call concealed chronic alcoholism. The obvious case of addiction to alcohol can hardly be excluded from the study until the diagnosis is actually made by the surgeon treating the patient. Then the diagnosis chronic alcoholism is added to the surgical diagnosis.

The need of recognition of all types of alcoholism in patients with surgical conditions is emphasized and illustrated in certain cases which I have observed and which I shall describe. In this report the term concealed chronic alcoholism is used for the first time so far as I know. If there is a condition deserving the name concealed chronic alcoholism, there are, I believe, means of making the diagnosis. Some of these are herein detailed.

Acute alcoholism is as a rule comparatively easy to recognize except when such severe conditions as coma have supervened. In many cases of glandular imbalance, organic disease and trauma, the odor of alcohol on the breath may mislead the examiner. The further examples of tumor or abscess of the frontal lobe, insulin shock, diabetic ketosis, uremia and various injuries of the skull need only to be mentioned to remind one that a complete analysis of every case is necessary to avoid attributing to alcoholism the symptoms of some other condition.

A patient who is a victim of true chronic alcoholism may show no clearcut signs if the taking of the history, the physical examination and the laboratory analysis are carried out in a cursory manner. A list of all the findings in a questionable case, however, should furnish clues by which to reach the diagnosis of acute or chronic alcoholism or concealed chronic alcoholism.

The most common symptoms of true alcoholism are the following: tremors of the eyelids, tongue, the facial muscles, hands and even legs; erythema or flushing of the face, or sometimes pallor; acne-like cutaneous eruption of the face; telangiectases of the face; atrophy of the limbs; obesity or emaciation; poor muscular coordination; evidence of peripheral neuritis; disorientation; hypoesthesia; paresthesias; "fatty heart";

hypertension; albuminuria; venous engorgements, especially of the head; headache; mental depression; dizziness and vertigo; irritability and restlessness; insomnia; polyuria; tachycardia; tinnitus; dyspnea; palpitation; precordial pain; physical and mental weakness; moral deterioration; delirium tremens; gastric upsets; colitis; constipation and variable appetite for certain foods; dysphagia; hoarseness, and even purpura and cirrhosis of the liver.[1] Some of the pigment changes seen in the skin of drunkards are unquestionably due to the intake of alcohol.[2]

The characteristic appearance of the person with alcoholism varies even with the time of day as well as with many other factors.[1]

If the surgical condition is difficult to diagnose or the diagnosis is questionable, it is imperative that the examiner keep in mind the possibility of alcoholism. It is when this is neglected or forgotten that the condition is wrongly diagnosed and the patient allowed to follow his course precariously, often approaching a state of depression, near mania or even delirium tremens.[3] There is, then, a logical reason to be aware of the possible presence of alcoholism, because trauma or elective operation, as well as minor operations, can precipitate trouble. Even more important is it to diagnose what I believe should be called concealed chronic alcoholism, for in such a case the surgical treatment must be individualized. The patient must be studied as presenting a psychologic,[3] if not a medicolegal, problem.[1] He should undergo general and special routine examinations, and such examinations should be a part of the surgeon's procedure. Until further evidence has developed as to the scope of the term concealed chronic alcoholism, any case of alcoholism in which the diagnosis is not made at the time of onset of the surgical condition may be considered justly one of concealed alcoholism.

DIAGNOSIS

The diagnosis will be obtained from (*a*) the information offered by the patient's relatives, (*b*) the history related by the patient, (*c*) the results of the routine examination of the patient and (*d*) the results of special examination of the patient, as well as of laboratory tests.

If the examiner finds the patient unnecessarily hasty, he should always impress on him and his family the importance of the questions

1. Crothers, T. D.: Inebriety: A Clinical Treatise on the Etiology, Symptomatology, Neurosis, Psychosis and Treatment and the Medico-Legal Relations, Cincinnati, Harvey Publishing Company, 1911.

2. Iida, Y.: Influence of Aliphatic Alcohols upon the Pigment-Excreting Function of the Liver and Kidneys: A Comparison of the Effects of Aliphatic, One-Basic, Saturated Alcohols, Jap. J. Gastroenterol. **8**:179-186 (Dec.) 1936.

3. Kelly, J. A.: Post-Operative Psychoses, Am. J. Obst. & Gynec. **59**:1035, 1909.

and the need of care in uncovering all pertinent facts. Often when the physician insists on all details and explains that nothing can, or will, be done until the routine of taking of the history is complete, the patient will reverse his attitude and proffer information which he at first withheld. The history taking must not, however, be prolonged in an unwarranted way. The amount of questioning will vary in each case.

Methods of interrogating the patient hardly appear to call for detailed description, but because of the variability in examiners' methods, in the findings and in the cooperation of patients, certain points should be emphasized.

Standard questions should be put, and they should be asked with authority. The physician must learn the exact amount of alcohol taken in a given length of time, whether it was by the day, the week, the month or the year. Persistence will nearly always bring out unexpected facts.

The connotation word "routine" as applied to the examination of a patient depends on the severity and location of the lesion calling for surgical intervention. The complete routine examination, not excluding a neurologic examination, includes a record of the findings from head to foot. An exact rule cannot always be followed. It is advisable to make examinations always in the same way. When the order must be changed or a part of the examination delayed, repeated examinations should be regularly carried out. Methods of charting should be uniform. In some hospitals it is already a routine to make uniform records of all patients because in the past delays in taking histories and irregular charting of incomplete information have led to distressing legal difficulty.

During the entire so-called routine examination the examiner should be on the watch for evidence of concealed chronic alcoholism, especially if the history is suggestive. Education as to what to look for must vary with the examiner and the practice.

The special examination of patients suspected of alcoholism will of course be a part of the conscientious physician's routine. Eventually there should be no need to differentiate these two parts of the investigation. For the sake of emphasis I shall group certain aspects of the total examination under the head of special examination.

The special examination must be undertaken with alcoholism in mind, either at the time of the routine examination or immediately afterward. The order of examination should be uniform. The examiner may begin with the head and end with the extremities, or he may use any order of search that includes all the systems, that is, the skin, the bones and joints, the circulation, the respiration, the digestion and the nervous system. In addition, there should be a brief but conclusive summation

of the history and findings. This will bring out considerations that might otherwise be overlooked.

The signs to look for are many. The examiner should recall that the effects of alcoholism may vary. The condition may at times be associated with or cause, possibly only indirectly, the following changes: (1) premature age (gray hair, obesity and sedentary habits); (2) cutaneous changes (atrophy, venous engorgements, telangiectases, acne-like lesions, erythematous eruptions and other changes of color, such as pallor or yellowness, and, rarely, even purpuric changes); (3) metabolic changes, some temporary and others definite and permanent; in all probability, arthritis, dermatoses not already mentioned and cardiac symptoms (if not definite cardiac disease); (4) possibly, renal and hepatic disease, diseases of the blood-forming organs or of the glands of internal secretion; also, diseases of the central nervous system as well as peripheral neural involvements, and (5) mental and moral deterioration when truly gross changes in the nervous system have not yet occurred.

Any one who wishes to question these statements may do so, but no one can deny that thousands of patients have been observed who presented many degrees of these changes with no fact available clinically to explain their conditions but the definite history of an intake of alcohol. Unfortunately the lack of total abstainers as controls for the determination of the diseases related to alcoholism prohibits final conclusions.

If one examines persons with acute alcoholism, however, one cannot deny that (*a*) such patients may have intense nervous exhilaration from release of the higher centers or they may have depression of such severity as to cause cyanosis affecting the metabolism of the entire body, even enough to cause death; (*b*) they may react to alcohol according to known variants or they may manifest tolerance—a state observed clinically though not yet demonstrated by laboratory and other scientific tests;[4] (*c*) they may at times exhibit an unexplained susceptibility to alcohol.[5]

The action of alcohol appears to be incompletely understood, but this does not mean that its effects can be omitted from consideration.[4]

The special examination, then, if carefully performed, will often reveal numerous abnormalities. Many of these can be ascribed to factors other than alcoholism, but this, of course, should not exclude them from consideration.

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4. Newman, H., and Card, J.: Nature and Tolerance to Ethyl Alcohol, J. Nerv. & Ment. Dis. **86**:428-440 (Oct.) 1937.

5. (*a*) Silkworth, W. D.: Alcoholism as a Manifestation of Allergy, M. Rec. **145**:249-251 (March 17) 1937. (*b*) Strean, L. P.: A Case of Angioneurotic Edema from Alcohol, Canad. M. A. J. **36**:180-181 (Feb.) 1937. Crothers.[1] Iida.[2] Newman and Card.[4]

In the description of cases which follows, the details of the histories and examinations will be instructive in pointing out ways to ennance a routine examination.

As yet there is no practical or universally approved test on the result of which one may base an absolute diagnosis of chronic alcoholism, and undiagnosed alcoholism is rarely mentioned in the literature.[6] Tests for alcohol in the blood of persons under or recently under the effects of alcohol are advocated but are not yet in use in most hospitals.[7] So far, then, the only tests available to the physician are: tests for the chemical composition of the blood, tests for metabolic function, various blood counts, analyses of secretions (exclusive of their alcoholic content) and a few tests for vitamin deficiencies.[8]

Almost any laboratory test may be indicative of disturbed function, which in turn may be partly due to the effects of alcohol.[9] Such tests can be done when necessary to determine the presence of such conditions as disturbed metabolism, anemia, nephritis and hepatitis.[9]

A gastrointestinal series of roentgenograms taken after administration of a barium sulfate enema seems to me of value in pointing out early an abnormality of function in the digestive tract, particularly stasis, which is at times associated with chronic alcoholism.

Although an intelligence test may be a far cry from the surgical condition at hand and from the condition of concealed chronic alcoholism that is suspected, I wish to suggest that such a test be made. The careful examiner does, as a matter of fact, observe the mentality of all patients at all times, but the results are not uniform unless a regular procedure is followed. Thus, under the pressure of interest in a surgical condition in the patient, the physician may not converse with him at sufficient length to notice his loss of memory for past events, his inability to orient himself or his inability to add a column of figures. Whenever relatives are unaware that there is a change in the patient or are reticent about volunteering such information about him or cannot be reached for questioning, it seems worth while to include the physician's opinion of

6. Dauphin, P.: Undiagnosed Alcoholism, Marseille-méd. **2**:597-639 (Nov. 15); 648-673 (Nov. 25) 1935.

7. Gettler, A. O., and Siegel, H.: Quantitative Isolation of Ethyl Alcohol from Tissues of Alcoholics, Am. J. Clin. Path. **7**:85-93 (Jan.) 1937.

8. Wright, I. S., and Lilienfeld, A.: The Pharmacologic and Therapeutic Properties of Crystalline Vitamin C (Cevitamic Acid), with Especial Reference to Its Effects on Capillary Fragility, Arch. Int. Med. **57**:241-274 (Feb.) 1936.

9. Chiray, G. A., and Deparis, M.: Diagnosis of Acute Hepatitis in Chronic Alcoholism by Test of Provoked Galactosuria, Arch. d. mal. de l'app. digestif **26**: 481-526 (May) 1936. Guillot, M., and Gwan, O. S.: Inhibiting Action of Alcohols on the Action of Acetylcholine and Histamine on the Isolated Intestine of the Guinea Pig, Compt. rend. Soc. de biol. **125**:33-35, 1937.

the patient's mental and moral status as one result of the special examination. I do not wish to imply that the physician should always suspect a brilliant student of dementia or a prominent executive of Korsakoff's syndrome; yet the occurrence of a sudden surgical calamity may temporarily blind the casual examiner unless definite questioning and deduction along this line are included in the special examination.

I wish to present now a few case histories in sufficient detail to illustrate the points I have mentioned. The patients were encountered in my own practice. Some, if not all, should be considered as presenting true alcoholism, describable as concealed chronic alcoholism only because of the delay in the recognition of the most important facts uncovered in the histories, examinations and certain tests. A few are possibly to be considered as having true concealed chronic alcoholism.

REPORT OF CASES

CASE 1.—A man aged 32 was admitted to the New York Post-Graduate Medical School and Hospital on Aug. 2, 1936. The patient was a Southerner and apparently well to do.

Family History.—The father died when the patient was very young. There was one brother, who was in only fair health and was a "heavy drinker." The mother was living and well, aged about 65.

Marital History.—The patient had been married twice. He was divorced from the first wife and was separated from the second after seven years of marriage. There were no children.

Past History.—The patient had had typhoid at the age of 13 and pleurisy at the age of 26 and at the age of 30. When he was 28 years old, the tonsils and adenoids were removed and circumcision was done. Three operations had been performed for hemorrhoids, at the ages of 24, 25 and 29. At the age of 30, he had had phlebitis in the right leg, requiring rest in bed for six weeks. The leg swelled to twice the normal size, and the condition was supposed to have been caused by repeated sprains of the right ankle, suffered while the patient, intoxicated, was playing golf in the rain.

Habits.—He had smoked two and one-half packs of cigarets a day for years. His intake of alcoholic liquor had been constant for years in slightly varying amounts, with a few intervals (months) when only beer was taken.

Occupation.—The patient had never been employed except temporarily, for a few months, on one job.

Present Ailment.—Pain had been present in the right leg for months and had been especially severe the last week or two. The patient had been treated for thromboangiitis obliterans by diathermy, baths, suction boot and other means, without relief. He had had so much pain in the week prior to admission that he had done little but drink malt and spirituous liquors. He insisted that the leg was normal after the recovery two years before. He said he had taken no food for a week.

Physical Examination.—The patient was a well nourished though somewhat ill man. He appeared to be well oriented and to realize somewhat the serious-

ness of his condition. He complained of intense pain in the right leg and made no effort to use the extremity. He guarded it from any contact, even with soft blankets.

Head and Neck: The hair was somewhat untidy, although it had been recently cut; the scalp was in good condition. The skin of the face was slightly mottled with erythematous areas of slight extent. The airways of the nose were open, but there was a deflection of the septum. The breath seemed alcoholic. The eyes were not remarkable, though slightly bloodshot. There were tremors of the eyelids and the tongue. The teeth were dirty and discolored, out of proportion to the patient's age and social station. The throat was red. The tongue was dry, clean and thick. There was a strong gag reflex. The chin was receding and the lower lip somewhat infolding along the crease, 1 cm. below the vermilion border. A short moustache covered the upper lip. The external ears were of fair color only. The skin of the face was closely shaven. The neck was not remarkable but was somewhat flabby. No lymph nodes were palpable, and the thyroid was not felt. Close examination showed a somewhat rapid beat in the slightly pulsating cervical vessels.

Chest: The chest showed nothing remarkable. The muscular development was not unusual. The skin seemed flabby, and there was a layer of fat over the muscles. The heart sounds were characterized by slight softness and faintness. The pulse rate varied from 96 to 110. The blood pressure was 100 systolic and 70 diastolic.

Abdomen: The abdomen was slightly obese, but the only abnormal finding was muscle spasm in the lower quadrants, especially above Poupart's ligament on the right side. The pulse of the right femoral artery and that of the right external iliac artery could not be made out. The genitalia were normal. Rectal examination showed spasm of the sphincter and evidence of scarring. There was slight protrusion of the rectal mucosa, and the patient refused further examination than that gained by reinserting the prolapsed hemorrhoid.

Extremities: The arms were well proportioned and fairly well developed, and the hand shake revealed a soft, pliable hand. The hands were moderately well cared for. The fingers were nicotine stained, and there was a tremor of the outstretched fingers. The right leg was paler than the left; it was cold and was hypersensitive throughout its length. No pulse was palpable in the femoral, popliteal, dorsalis pedis or posterior tibial vessels. The severity of the condition did not warrant oscillometric readings at this time. There were no ulcerations of the bottom of the foot, along the anterior transverse arch or on the lateral side of the sole. The left leg showed diminution if not absence of the dorsalis pedis and posterior tibial pulses, although the popliteal and femoral pulses were strong. The left leg was warm, and except for the callus over the outside of the sole and ball of the foot showed no abnormality, unless the slightly pink toes might have been considered abnormal. The return of circulation to these toes after squeezing was immediate.

Laboratory Observations.—On August 3 the red cell count was 4,880,000; the white cell count was 11,000; there were 71 per cent polymorphonuclears. The bleeding time was four minutes and the coagulation time four and one-half to six minutes. A platelet count on a later date was 200,000. The nonprotein nitrogen content of the blood was 29 mg., that of urea nitrogen 7 mg., that of sugar 80 mg. and that of chlorides 545 mg. per hundred cubic centimeters. The carbon dioxide–combining power was 56. The urine was acid and had a specific gravity of

1.012; otherwise the results of urinalysis were negative. On August 7 the carbon dioxide–combining power of the blood was 48.5; the inorganic phosphate content was 4.7 mg. and the calcium content 11.3 mg. per hundred cubic centimeters. The Wassermann reaction of the blood was negative. Oscillometric readings on August 6 showed no excursion of the needle in connection with the right leg or thigh and slightly diminished excursion in connection with the left thigh and lower third of the leg. The readings for the upper and lower parts of the arms were satisfactory. The patient's blood was of group III (Jansky). The return of circulation after elevation of the right leg for two minutes required twelve seconds, but on the left when observation was made of the color of the toes on August 6, the return of circulation was only slightly delayed. The pulses in the left foot were felt easily on August 7. Repeated Landis tests showed no change of temperature in the right foot after immersion of the arms in hot water (above 110 F.) for thirty minutes or more, nor sweating of the right leg below the ankle. The left leg reacted normally.

On September 8 roentgen examination of the chest showed chronic root, branch and central bronchial thickening, with moderate dilatation toward the bases of the lungs.

On September 8 an electrocardiogram showed only a fast auriculoventricular rate of 112.

On October 2 the basal metabolic rate was +26 per cent and on November 4 it was +14 per cent.

Treatment.—Conservative treatment included: regular diet; low protein diet; forcing of fluids; infusions of physiologic solution of sodium chloride and of 5 per cent solution of sodium chloride; transfusions of female blood; administration of vitamin concentrates; general massage, catharsis; colonic irrigations; application of dry mild heat from an electric light bulb cradle; use of infra-red rays; elevation of the legs and hanging down of the legs over the side of the bed, and therapeutic use of Landis tests. Also, typhoid vaccine fever therapy (with estradiol benzoate) and treatment with "carnacton," insulin and insulin-free pancreatic tissue extracts were tried. In addition, a daily allowance of whisky was given, and calcium lactate, sodium salicylate, spasmalgin (an opium-atropine preparation) and sodium iodide were tried. Finally bromides, phenobarbital, codeine, morphine and atropine were given before conservative treatment was abandoned, on September 5.

Operative treatment consisted of midthigh amputation of the right leg, performed by the method of enucleation on September 5, with the patient under ether anesthesia.

Postoperative treatment included administration of morphine, codeine, phenobarbital and small portions of whisky (which the patient supplemented with repeated additions from his own sources in spite of surveillance). He was discharged from the hospital on October 11, with a healed amputation stump in excellent condition.

Comment.—This case contains a lesson for all surgeons who are confronted with patients who admit consumption of alcohol but appear so cooperative and so ill from their surgical condition that their faces and manners belie their true history and the condition of chronic alcoholism. The alcoholism in this patient was not difficult to diagnose except that its significance was probably underestimated until he suffered from a condition calling for surgical intervention. Every one who saw

the patient remarked after a few days of conservative treatment how much he had improved.

The nurses, however, soon discovered him in lies about smoking and drinking, against orders. This was amply borne out by his subsequent misstatements to the examiners. Fortunately, the contact between the staff and the patient was sufficiently close and often repeated to engender mutual respect. It was possible, then, to get fair cooperation from the patient, considering his reputation for emotional imbalance and drunkenness.

However, after the patient recovered from the operation and the stump was healed, his cooperation lessened considerably. His desire to maintain a reasonably clean and moral life appears from reports to have faded. It is noteworthy that he spent a good many of his years in the company of the patient in case 5 under much the same conditions of self indulgence.

Summary.—Every paragraph under the detailed history records observations obviously pointing to a diagnosis of alcoholism. These are supplemented by details of physiognomy and results of physical examination, as enumerated. The therapeutic administration of alcohol appeared to be helpful.

CASE 2.—A man aged 41, American born of Italian parents, was admitted to the New York Post-Graduate Medical School and Hospital on Nov. 29, 1935.

Family History.—The facts are irrelevant except that extreme poverty and poor home conditions prevailed during the patient's youth. The patient's father was a drunkard.

Marital History.—The patient had been married eight years. His wife was strong and well. There was one son, living and well.

Past History.—The patient had suffered several injuries at work during a period of several years. One of these injuries consisted of multiple fractures of the ankle, necessitating a period of hospitalization. The last injury had occurred within the past three years. There had been no operations with the exception of repair of the distal phalanges of the right thumb and forefinger during childhood. He recalled the usual children's diseases as having occurred without complications.

Habits.—The patient admitted a variable intake of alcohol for many years, and he smoked constantly. His wife amplified the story by saying he "is a terrible drinker when he gets started."

Occupation.—The patient was a structural steel worker.

Present Ailment.—In the patient's own words, "At 10 a. m. the snap of the riveting gun broke, and the plunger of the gun hit my right big toe. I worked until 4 p. m. but had to stop on account of pain which I could not stand any longer."

Physical Examination.—Examination revealed a nervous, highly excitable man, who appeared to be in pain but was otherwise healthy and cooperative. The temperature was 97 F., the pulse rate 72 and the respiratory rate 20.

Head and Neck: The hair was thick, unruly and black, beginning to turn gray; there were no abnormalities of the eyes, nose or ears. The teeth were in

fair condition. The tongue was slightly coated. The tonsils were atrophic. The throat was not inflamed. The neck was thick and short but otherwise normal. The face was coarse and the facial features thick and heavy; the eyes were sharp and dark.

Chest: The blood pressure was 140 systolic and 90 diastolic. The chest was rounded and barrel shaped. No abnormality of the heart or of the lungs could be made out through a very thick chest wall.

Abdomen: The abdomen was obese, presenting no other abnormality; the genitalia were normal. Rectal examination was not done.

Extremities: The extremities were short, heavy and well developed. The right great toe was swollen to about one and one-half times its normal size. It was bluish at the base of the nail, and there was a slight abrasion of the skin at this point. There was abnormal motility between the distal and proximal phalanges. There was variable but slight tenderness over the tarsus; this was not definitely localized. The legs were short in proportion to the body.

Laboratory Observations.—The results of urinalysis were normal. The blood count showed: red cells, 5,700,000; white cells, 10,000; hemoglobin 98 per cent; polymorphonuclears, 54 per cent. The Wassermann and Kahn reactions were negative. The nonprotein nitrogen content of the blood was 45 mg., the urea nitrogen content 15.2 mg. and the sugar content 95 mg. per hundred cubic centimeters. The roentgenogram showed a fissure fracture of the base of the distal phalanx of the right great toe, in good position.

Treatment.—Treatment consisted of application of a plaster cast from beyond the end of the toes to the midportion of the lower part of the leg for fourteen days, followed by use of an iron plate in the shoe for several weeks. Hospitalization was of two weeks' duration. The patient was allowed out of bed after the first day and was given the regular diet after the second day. Whisky was supplied on two or three occasions on the second and third days because of his extreme restlessness and irritability and also because of a rise of the temperature to 100 F., a rise of the pulse rate to 96 and my belief that he was faced with the onset of delirium tremens.

Comment.—The patient was difficult to handle from the beginning, and his suffering seemed out of proportion to his injuries. His requests to return home and start work could be met only by the application of a heavy, unwieldy cast sufficient to impress on him his helplessness and need for care. His insomnia and bad behavior in the ward would have jeopardized the healing of his fracture with any other treatment than a heavy cast, for he got up several times without permission during the first night or two and stumbled about in the dark. The high nonprotein nitrogen content of the blood was determined after I had observed some edema of the left ankle several days after his admission. The patient then admitted that he had noted attacks of edema of the ankles during the last year or two, after drinking beer. It is decidedly questionable how the patient would have reacted had he not been given the two or three doses of whisky when he was most obstreperous.

Summary.—The history was suggestive of alcoholism, and the presence of the condition was admirably proved by the behavior and

physiognomy of the patient, and by the physical signs, as well as by the good results of alcoholic medication.

CASE 3.—A white man aged 29 was admitted to the Broad Street Hospital on Jan. 20, 1937. He was seen for the first time by me twelve hours after a drinking bout, with a 4 inch (10 cm.) irregular laceration and other smaller lacerations of the scalp, one stab laceration of the right forearm and numerous scratch abrasions of the body. He was completely sober and stated that he knew nothing about having been injured until he awakened in the morning and found himself bleeding from his scalp.

Family History.—The father died at the age of 58, and the mother was living and well at the same age. Two sisters were living and well. One uncle, aged 68, had diabetes.

Marital History.—The patient had been married nine years. There were no children. He had been temporarily separated from his wife but the couple had been reunited several times.

Past History.—The patient had had pneumonia at 16 and tonsillitis at 23 (requiring hospitalization), and he believed he had had measles, mumps and whooping cough, but he was not sure. There had been no operations except a repair of a laceration of the lip at the age of 14. There had been no other accidents except a fracture of the ankle at the age of 18, which had caused him no trouble since.

Habits.—He had smoked more than a pack of cigarets a day for years. His intake of liquor was variable but immoderate except during the periods when he abstained completely.

Occupation.—The patient was a commission bond salesman in a large Wall Street firm.

Present Ailment.—There were multiple injuries, including lacerations of the scalp and of the right arm and abrasions and contusions of the body.

Physical Examination.—The patient was obese, appearing several years older than his age. His light blond hair was cut short and was matted with dried blood. From the expression of his face and the bloodshot eyes it appeared that he had been drinking. He was cooperative and somewhat nervous and concerned about his condition. He was completely oriented and intelligent and was impatient to be treated. The temperature was not elevated; the pulse rate was 100 and the respiratory rate 18.

Head and Neck: The scalp was lacerated with an irregularly shaped wound in the left anterior parietal region, approaching the midline. This wound was at least 4 inches (10 cm.) in length. There were three other small superficial lacerations of the scalp; one in the right parietal region, another in the left upper temporal region, and one posteriorly, in the occipital region. There was no blood in the ears, nose or mouth.

The nasal septum was deflected. The external canals in both ears were somewhat irregular in contour because of exostoses. The ear drums were retracted. The hearing in the left ear was considerably diminished. The eyes showed no abnormalities except slight redness or injection of the small vessels of the tarsal and bulbar conjunctiva. The teeth were discolored to a degree out of proportion to the patient's age and social status.

The tonsils were scarred and red from chronic infection along the anterior pillars. The submaxillary lymph nodes were palpable in a somewhat obese neck.

The features were coarse, and the patient looked like a person with chronic alcoholism.

The thyroid was not palpable. There was no stiffness or tenderness of the neck.

Chest: The blood pressure was 125 systolic and 90 diastolic. The heart and lungs presented no abnormal physical signs. The skin of the chest anteriorly and posteriorly was marked by long scratch abrasions in various directions, all superficial.

Abdomen: The abdomen was obese but presented no other abnormality except scratches similar to those on the chest. The genitalia were normal. Rectal examination was not done.

Extremities: The limbs were fairly well developed and somewhat obese. They presented no abnormalities except for scratch abrasions on the arms. There was an avulsed stab laceration at the lateral end of the antecubital crease, at the junction of the upper part of the right arm and forearm. The edge of skin lacerated at this point was about 3 inches (7.5 cm.) long, and the cut was in the shape of an acute angle with its apex pointed toward the shoulder. There were gross tremors of the outstretched hands. There was no paralysis of either hand.

Laboratory Observations.—Laboratory tests, including the Wassermann and Kahn tests, showed no abnormality. The blood counts were normal. Urinalysis at the time of entrance to the hospital gave negative results except for the presence of 1.4 per cent sugar by the quantitative Benedict determination. Roentgenograms of the skull showed it to be normal, and the sugar content of blood taken the day after the patient's entrance into the hospital was 90 mg. per hundred cubic centimeters, with the patient fasting.

Treatment.—Treatment consisted in débridement and repair of the lacerations of the scalp (after careful hemostasis) and a plastic repair of the laceration of the right arm. The patient proceeded from fluids to the regular diet within three days, and except for nervousness, irritability and restlessness, which were relieved on the third night by 2 ounces (60 cc.) of alcohol, he was easily handled by oral administration of amytal and phenobarbital.

Comment.—The patient when first seen (in his apartment) was hard to handle. He refused to enter the hospital until he had practically fainted in an attempt to prepare himself to undergo the suturing of his wounds at home. He could be persuaded to go to the hospital only with the promise that he could also have his tonsils removed after a day or two. In the hospital, at the end of about six days, when it was believed reasonably safe to consider a tonsillectomy, he refused this procedure. He also refused narcotics, and it is my belief that the good night's rest on the third night, after two nights of poor rest, was probably determined by the intake of a small amount of alcohol that evening.

Summary.—The marital history, the habits and the recent drinking of alcohol should be emphasized. The physiognomy and some of the physical findings may be significant. As the patient refused narcotics, he was difficult to manage until whisky was given him.

CASE 4.—A white man aged 43 was first seen by me on March 5, 1936.

Family History.—The father died at the age of 30, of a long illness of unknown nature. The mother committed suicide at the age of 51. Two brothers were

living and well. One brother died at the age of 6 months, of unknown cause. There were no sisters. The patient's mother had been temporarily insane after childbirth and had been committed to an asylum.

Marital History.—The patient had separated from his wife after several years of marriage.

Past History.—The patient had had gonorrhea in 1929 with no further difficulty until there was a slight discharge from the urethra three months prior to examination. There had been a bullet in the left knee since the age of 14—an accidental injury. Roentgen examination had been done for possible ulcer at the age of 32; the patient had dieted for fourteen days and had had no pain since. He stated that it was his habit never to eat fried foods. He had been told that his appendix appeared webbed on roentgen examination. He had known of a growth on the right tonsil for a long time.

Habits.—The patient had been a consistent drinker of beer since before prohibition and had "suffered slight dizziness for years and a feeling of falling." He was a heavy smoker of cigarets.

Present Ailment.—There had been nervousness over his health for several weeks. He complained of a urethral discharge, which had been present for three months, of slight pain in the right side of the abdomen, present for three or four days, and of nocturia, which occurred about once a week.

Physical Examination.—The patient was a nervous, pallid, well nourished, cooperative, intelligent and respectful man who appeared to be about the age he claimed (43); he seemed slightly and chronically ill but active and well oriented. The temperature was 99 F., the pulse rate 84 and the respiratory rate 18.

Head and Neck: The hair was slightly thin; the eyes were alert; there was no abnormality except slight lid lag. The ears were essentially normal. The nose showed defection of the septum; the teeth were discolored, decayed and in need of immediate attention. The thyroid was palpable, small, firm and deeply placed. The submaxillary glands were palpable. There was an almond-shaped and almond-sized polyp of the right tonsil. Both tonsils were large and deeply placed and were slightly red along the anterior pillars.

Chest: The blood pressure was 130 systolic and 80 diastolic. The heart and lungs revealed no abnormality. The skin of the upper sternal region was slightly rough.

Abdomen: The abdomen was slightly obese. Rectal examination disclosed no abnormality except that the prostate was slightly enlarged and boggy but not tender. Examination of the genitalia showed a long prepuce and a moderately profuse seropurulent urethral discharge.

Extremities: There was a scar on the medial side of the left knee. There was a marked tremor of the extended fingers. The knee jerks were hyperactive.

Laboratory Observations.—The Wassermann and Kahn reactions were negative.

Treatment.—Therapy consisted in forcing of fluids, local hygienic treatment of the redundant prepuce, and administration of bromides by mouth and of acetylsalicylic acid for the focal infection in the mouth. A few days later, after roentgen study had shown that the roots of the teeth were grossly infected, the patient had several teeth extracted by a reputable dentist. Six hours after the extraction, he suffered a moderately severe hemorrhage, for which he had to be treated in an out-of-town hospital. Recovery after the hemorrhage was gradual but satisfactory. The patient has had further teeth extracted at intervals during the past year without mishap.

Comment.—The danger of hemorrhage in a patient who may have chronic alcoholism should not be overlooked, in spite of the well known fact that both hemorrhage and infection are common in persons who have several badly infected teeth removed at once. In the case reported here, multiple extractions should not have been done without safeguarding the patient against such consequences. It is well to remember that this patient might have been given considerable comfort after the operation by the administration of a small amount of alcohol and that the anxiety aroused by the considerable hemorrhage might better have been treated prophylactically by a stay in the hospital after the extraction, which would have guaranteed a night or two of sleep under ideal conditions.

Summary.—The bad family history, the suggestive marital maladjustment, the past history of the patient, his habits and his symptoms all indicated concealed chronic alcoholism, which was further to be suspected from the patient's physiognomy and behavior and from the physical findings and the course of the illness. Alcohol was not used therapeutically in this case.

CASE 5.—A white man aged 36, a Southerner, was seen once, Sept. 1, 1936.

Family History.—The father died of pneumonia at the age of 50; the mother was living and well at the age of 50. The patient was an only son. A first cousin had thromboangiitis obliterans.

Marital History.—The patient was divorced after having been married for several years. He had a daughter.

Past History.—The patient had had scarlet fever at the age of 16. He had had measles, mumps and jaundice as a child. At the age of 29 the tonsils had been removed because of recurrent sore throat. All the upper teeth had been extracted. Fracture of the left clavicle had occurred at the age of 30.

Habits.—The patient had smoked steadily since the age of 13 and had drunk beer and liquor since the age of 17.

Occupation.—He had no occupation at this time, although he had graduated from law school, passed the bar examinations, and practiced law a short time in his home town.

Present Ailment.—The patient complained that he had suffered from pain in the calves for one year and from burning of the feet for many years, with relief on removal of the shoes. He had had difficulty with the feet when in the army. He described an intermittent feeling of fatigue and heaviness, without cramps but with some ache above the knees and in the calves during the last year. This was immediately relieved by rest.

Physical Examination.—The patient was a hollow-eyed brunet of good education, thin but fairly healthy. The temperature was normal. The pulse rate was 90 and the respiratory rate 18.

Head and Neck: There were no abnormalities of the head and neck with the exception of chronic nasopharyngitis. The upper teeth had been removed. The remaining teeth were in poor condition. The tonsils had been removed.

Chest: The blood pressure was: 120 systolic and 80 diastolic. The heart and lungs presented no abnormalities.

Abdomen: The abdomen was soft and flabby, not obese but slightly prominent as compared with a somewhat flat chest. The liver, spleen and kidneys were not palpably enlarged. The genitalia were normal. Rectal examination was not done.

Extremities: The arms were normal. The legs were well developed though somewhat thin. The popliteal, dorsalis pedis and posterior tibial pulses were not as easily felt on the left as on the right. Especially was this true of the dorsalis pedis pulse, which at times was difficult to make out at all.

A tentative diagnosis of thromboangiitis obliterans was made, and the patient was advised to discontinue smoking. He was instructed to return for further diagnostic tests and the outlining of treatment. He was afterward seen nonprofessionally, when he admitted that he could not stop smoking and that he had done considerable heavy drinking. He did not think he would bother with further diagnosis and treatment.

Comment.—It is interesting that this patient showed the clinical symptoms of early arteritis obliterans and gave some evidence of the disease. Significance may or may not be attached to his long association with the patient in case 1 (since childhood) and to the fact that he had a first cousin with a circulatory difficulty of the legs, which had been pronounced thromboangiitis obliterans. All 3 of these persons were young men about the same age (in the thirties) who had led a similar life in the same town. At the time of writing the patient seems likely to follow a course similar to that of the patient in case 1.

Summary.—The similarity to case 1 is obvious—marital difficulties, a past history of consumption of much alcohol and the history and findings of circulatory disease of the extremities. The lack of psychic stamina, as shown by the patient's lack of interest in his own future when his friend had recently lost a leg from a disease perhaps similar to his own, gives an idea of the lack of hope in some of the cases of this type. The family, past, marital and other history was indicative, as were the ailments presented, the physical findings, the known pathologic course and the patient's admitted inability to abstain from alcohol. Alcohol was not prescribed in this case.

CASE 6.—A woman aged 61 was first seen by me about 1 a. m. on Jan. 24, 1935.

Family History.—The family history was not detailed, but the facts given were essentially irrelevant.

Marital History.—The patient had been married approximately thirty-five years. She had had no children.

Past History.—She had had disease of the gallbladder four or five years prior to examination. This was cured with conservative treatment.

Occupation.—The patient was a housewife who had done literary work.

Habits.—There was no history of intake of alcohol.

Present Ailment.—The patient complained of loss of function, pain, swelling and abnormal mobility of the upper end of the left arm and shoulder. She had

received an injury while riding on a railroad train the same evening, January 23, about 7 p. m., when she was thrown out of her seat by the sudden jolt of the car. The patient refused first aid treatment and took a car back to the city of New York from several miles out in New Jersey, where the accident happened. She had had no food, medication or treatment up to the time I saw her, at 1 a. m.

Physical Examination.—The patient was an obese woman, nervous, pallid and in pain. She held her left shoulder with her right hand. Examination further than that necessary to determine abnormal mobility and distortion of the left shoulder joint was postponed until she was taken to the hospital.

Head and Neck: The hair was gray and somewhat thin. There was tenderness of the scalp over the occipital end and the parietal region. The ears were essentially normal. The upper and lower eyelids were puffy, and the patient complained of difficulty in keeping her eyes open. The pupils reacted poorly to light; accommodation was poor; there were some nystagmoid movements on looking to either side. The nose was thick and bulbous; the airways were fairly good. The gag reflex was strong. Many of the teeth had been removed. The tonsils showed no abnormality. The neck was obese and short.

Chest: The blood pressure was 170 systolic and 100 diastolic. The pulse rate was 100. No abnormalities of the heart or lungs were noted.

Abdomen: The abdomen was not examined particularly except for tenderness. Obesity prohibited palpation of any of the abdominal organs.

Extremities: The legs were obese; there were minor bruises of the lower part of the left leg. The knee jerks were variable. The right arm was normal; the left arm was swollen at the shoulder. There was abnormal mobility at the upper end of the left humerus, with crepitus and tenderness beneath the deltoid muscle. Motion at the elbow and wrist was normal. There was no nerve palsy.

Laboratory Observations.—A roentgenogram showed two lines of fracture of the left shoulder joint, involving the surgical neck and greater tuberosity of the upper end of the left humerus. Blood counts and urinalysis revealed nothing relevant.

Treatment.—Rest in bed, sedatives, light diet, and strapping and sling were used. Difficulty was encountered with the patient, especially after twenty-four hours, because of her nervousness, irritability, insomnia and general complaints of numerous kinds. She did not appear to improve even after a consultant was called, and she asked for a consultant of her own choice a few days later. This one advised the same treatment but immediately suggested that alcohol be prescribed at regular intervals. Physical therapy and early motion brought about an excellent result in the arm, but the patient's general condition was poor and her behavior untrustworthy for many months after the injury. She was seen by many physicians after her original treatment, which she followed out until March 22.

Comment.—Because of the patient's advanced years, marked obesity and nervous temperament she was difficult to handle. It is questionable how she would have done had she not been given alcohol daily at the suggestion of the second consultant, about a week after the injury. It was the opinion of this consultant that her denial of the intake of liquor was offset by her face, which could be probably characterized as coarsened and somewhat typical of the addict to alcoholic liquor.

Summary.—This case illustrates the advantage of complete history taking and examination. The past history and other data were of little

help. The outstanding characteristics of this patient were her coarse features, bad behavior and obesity. Alcohol was suggested by a senior consultant after only a moment's sight of the patient. Her course was satisfactory thereafter, although the handling of this patient was always a problem.

CASE 7.—A man aged 49 was first seen by me on Sept. 29, 1934.

The family history and the past history of the patient were not recorded.

Marital History.—The patient was not married.

Occupation.—He was in the advertising business.

Habits.—He had been a "heavy drinker and smoker" for many years.

Present Ailment.—There was loss of function of the left elbow since the patient fell in the bathtub on the day before examination. Pain on motion of the left elbow was noticed.

Physical Examination.—The patient was a rotund, large, obese, red-faced man, who appeared nervous.

Head and Neck: No gross abnormalities were noted except coarsening of the features, in addition to the high complexion. The neck was obese and short.

Chest and Abdomen: Examination of the chest and abdomen was not made, as the patient was ambulatory and there was no opportunity to carry out this examination.

Extremities: The legs were not examined. The left arm appeared normal in size except for slight swelling around the elbow. There was no abnormal position of any of the bones of the arm. The patient flexed the arm to an acute angle of about 80 degrees with considerable difficulty and allowed further flexion to an acute angle only after considerable argument, in spite of explanations and reasons for the need of this treatment.

Roentgen Examination.—The roentgenogram was not absolutely diagnostic but was suggestive of a chipped fracture of the medial epicondyle, without displacement.

Treatment.—The patient was instructed to keep the arm acutely flexed for at least two weeks. Instead, he consulted other physicians after a few days, who subjected him to physical therapy for two months before he recovered the use of his elbow.

Comment.—The patient was known to be chronically alcoholic, and his word was often untrustworthy. The fact that seven different physicians were consulted and the patient's own remarks a year or two later about the "joyride he went on with all the doctors," indicate the difficulty of managing this type of patient even if alcohol is prescribed.

Summary.—No further comment seems necessary except to emphasize the fact that only the most untrustworthy behavior may be expected of alcoholic patients, in spite of seemingly faithful promises, as in this case.

CASE 8.—A white man aged 36 was first seen by me on Oct. 15, 1936. He was admitted to the New York Post-Graduate Medical School and Hospital on October 27.

Family History.—Most of the facts were irrelevant. The father was living but diabetic at the age of 80.

Marital History.—The patient was divorced from his first wife; one son by the first marriage was living and well. The patient was living with his second wife. They had been married four years. There was one daughter by this marriage living and well.

Past History.—The patient had had gonorrhea over ten years previously. Two plastic operations had been performed on the nose within ten years.

Occupation.—The patient was a musician and arranger.

Habits.—He had partaken of liquor in variable but often large amounts for several years.

Present Ailment.—Pain in the right inguinal region had been present for four days. The only associated complaint was questionable: a slight urethral discharge a few days previously, which he attributed to overactive intercourse. He said that there had been a slight blister on one of the toes of his right foot several days before that, which was now healed. His general health had been good.

Physical Examination.—The patient was an obese, pale man of about the age stated, who appeared to be somewhat apprehensive but generally in good health. The temperature was 99 F. and the pulse rate 88. The respiratory rate was 10.

Head and Neck: The hair was reddish, long and worn smoothed close to the head. The eyes, ears and mouth presented no abnormalities. The nose was shortened, the airways narrowed and the bridge thickened. The nose was slightly aquiline.

Chest: The blood pressure was 130 systolic and 85 diastolic. The chest was somewhat obese. The heart and lungs presented no signs of abnormality.

Abdomen: The liver, spleen and kidneys were not felt. There was a small indirect inguinal hernia on the left side, easily reducible. On the right side the internal inguinal ring was relaxed, but no impulse was felt on coughing. There was an egg-shaped inguinal lymph node on the right side, deeply placed just above Poupart's ligament. It was acutely tender, and the skin over it was freely movable. The genitalia showed no evidence of any lesion. The prepuce was redundant but not inflamed. There was no urethral discharge.

Extremities: The arms were normal. The legs were well developed. There was no evidence of lesion on either foot. The mass in the right inguinal region enlarged continuously until October 27.

Laboratory Tests.—The urine was essentially normal.

Treatment.—Therapy was conservative until October 27, at which time the patient was removed to the hospital, and a large deep inguinal abscess on the right was incised and drained with the patient under ethylene anesthesia. Wet dressings and heat were applied to the wound. It was practically healed at the end of two months, at which time he was sufficiently well to go to another state and begin a new job. The wound was not completely healed, and in February 1937 it required cauterization of some granulations by a physician in another state. It healed completely shortly afterward and has remained healed to date.

Comment.—This patient was difficult to handle because of the chronicity and nature of his ailment. He was advised that alcohol might quiet his nerves. Alcohol was given on one or two occasions during his stay in the hospital, when he appeared to be most apprehensive. It is difficult to be sure, but it is my feeling that a large part of this patient's nervousness and irritability could be traced to his previous

intake of alcohol. The patient's general good health and urgent need to recover so as to be able to provide for his family probably aided the rather fortunate outcome. In a patient with less intelligence or willingness to cooperate the same surgical condition in the face of the definite, if irregular, alcoholic history might have had a different outcome.

Summary.—This patient suffered a long-drawn-out siege from a massive deep inguinal abscess. The past history, the habits and the marital and social history might have been suggestive of concealed chronic alcoholism. The exceedingly nervous attitude, the physical findings, the physiognomy and the actions of the patient in the hospital confirmed the diagnosis. He was apparently aided by the small amounts of whisky given him on a few occasions.

GENERAL COMMENT

The pathic person can be recognized at the time of the first examination if there is much disagreement between the history related by the patient and that furnished by others on questioning. It is a fact that in the case of the patient with a condition requiring surgical treatment who denies, understates or conceals his alcoholic habits, an unusual series of events often follows.

First, he will be found, sooner or later, to be untrustworthy. His word cannot be depended on. Second, complications or sequelae may occur that commonly do not occur in the case of the abstainer. Third, there will often be at some time in the course of his condition evidence of loss of cerebral stamina. A better way to express this would be to say that his nervous system may show instability at various points. The higher or the lower centers or both may show function completely different from that observed in most abstainers.[10]

The thousand and one ways by which a physician may gain objective signs of concealed alcoholism are often forgotten.[11] The simplest reason for this lies in the comparative superficiality of most routine clinical and even laboratory examinations of the patient with a condition calling

10. Knight, R. P.: Psychodynamics of Chronic Alcoholism, J. Nerv. & Ment. Dis. **86**:538-548 (Nov.) 1937.

11. (*a*) Cowles, E. S.: A New Pathology and Treatment of Chronic Alcoholism, M. J. & Rec. **133**:417-421 (May 6) 1931. (*b*) Villaret, M.; Justin-Besançon, L., and Klotz, H. P.: Fatty Degenerative Hepatitis as Prevailing Hepatic Lesion in Alcoholic Polyneuritis, Bull. et mém. Soc. méd. d. hôp. de Paris **52**:1159-1162 (July 13) 1936. (*c*) Baer, H. L.: Dermatitis of the Eyelids Due to Alcohol, Arch. Dermat. & Syph. **35**:291 (Feb.) 1937. (*d*) Baonville, H., and Titeca, J.: Abrupt Abstention from Alcohol as a Cause of Delirium Tremens: Twenty-Two Cases, J. belge de neurol. et de psychiat. **37**:135-154 (March) 1937. (*e*) Bersin, T.; Lanber, J. J., and Nafziger, H.: Effect of Anesthesia and Operation on Vitamin C Metabolism, Klin. Wchnschr. **16**:1272-1274 (Sept. 11) 1937. Crothers.[1] Knight.[10] Kelly.[8]

for surgical intervention. It is not customary to apply any test which measures the psychic stamina or the functional state of the nervous system. Still less commonly is it a practice to make any test of the blood to determine even acute alcoholism.[7] No consideration is given to such a test for patients with chronic alcoholism, because alcohol is so quickly eliminated from the body. Absolute lack of any clinical or laboratory test for unsuspected or concealed alcoholism makes a scientific approach to the whole subject at the present time practically impossible. Since alcohol is considered often in the same light as an anesthetic, vitamins C and B are worthy of consideration (Bersin and his associates).[12] Wright and Lilienfeld[8] and others[13] indicated latent deficiencies and need for increased vitamin intake. Anesthesia, infection and operation seem obvious[14] indications for such therapy.

Psychiatry has furnished the greatest contribution to physicians' knowledge of the intellectual state associated with both acute and chronic alcoholism. Many phases of functional mental disease have been at times related or at least attributed to either direct or familial intake of alcohol.[1]

In spite of all this, the surgeon repeatedly has had bad experiences with patients suffering from alcoholism of all types, especially those with concealed chronic alcoholism, because of the lack of a satisfactory clinical or laboratory test for the condition.

Occurrence.—Concealed chronic alcoholism is characterized by its occurrence usually in persons over the age of 18. The upper age limit is indefinite, but probably the condition is seldom seen in patients over 75. These extremes may seem extraordinary, but they can be explained.

There are no figures to indicate how many of the population have ever acquired a taste for alcoholic drinks, how many are absolute abstainers and how many may be considered more or less constant users of alcohol. Since some line must be drawn to differentiate the abstainer from the patient with concealed chronic alcoholism, true chronic alcoholism or any of the borderline conditions between these, practical if arbitrary rules must be set down.

True chronic alcoholism, in my opinion, may be considered to affect that person who is known to have consumed alcoholic liquors during at

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12. Leriche, R.: Hormonal Regulations in Surgery, Liége méd. **30**:876-886 (July 25) 1937.

13. (*a*) Lauber, J. J.: Vitamin Therapy in Surgical Diseases, Med. Welt **11**:415-420 (March 27) 1937. (*b*) Bridges, M. A.: Pre- and Postoperative Nutritional Regimen: Proposed Five Point Schema, New York State J. Med. **37**:2009-2012 (Dec. 1) 1937.

14. (*a*) Wechsler, I. S.; Jervis, G. A., and Potts, J. D.: Experimental Study of Alcoholism and Vitamin B Deficiency in Monkeys, Bull. Neurol. Inst. New York **5**:453-475 (Aug.) 1936. (*b*) Jolliffe, N., and Colbert, C. N.: Etiology of Polyneuritis in Addict, J. A. M. A. **107**:642-647 (Aug. 29) 1936.

least a year, daily, weekly or monthly, not more than ten years previous to the time of examination. It is rare, then, to consider a man as having true chronic alcoholism if he has not in the ten years previous to the time of examination consumed alcohol in moderate quantities for longer than one year.

More commonly true chronic alcoholism should be diagnosed if the patient partook of any form of liquor regularly for years, although he may not have tasted even beer for fifteen years.

Most commonly, true chronic alcoholism should be readily recognized in a patient who admits years of variable alcoholic intake up to the present, even if the intake is small or has occurred at intervals of as much as five years.

A chronically alcoholic person, then, should be considered as one who has had minimum habituation to alcohol in small quantities for as long as a few days only, or if at any time of his life he was given to a moderate intake of alcohol for at least a year, even if this occurred only once within a period of ten years. Conversely, a man who took only minute quantities of alcohol during one year within a past period of ten years probably should not be considered as having chronic alcoholism.

Concealed chronic alcoholism should be recognized in the person who has become inebriated more than three times in his life. Psychology has demonstrated that often the doing of an act three times makes it a habit, no matter how seldom that habit is manifested. It is probable, then, that a patient admitting inebriation three times in his life is chronically alcoholic, whether by habit or by minute physical change. Conversely, again, it is probably safe to absolve a person of true chronic alcoholism if strong evidence can be found to indicate inebriation on fewer than three occasions, in the event that there has been no intake of alcohol except on these occasions.

There is no need to describe the symptoms of what should be defined as acute alcoholism. These are all too well known. When doubtful, they merge into symptoms of true chronic alcoholism.

One or two borderline examples might be mentioned. A person was accustomed during a period of two years to accepting a sip of liquor when entertained at the homes of friends or in public but has not tasted even beer or wine for twelve years. This person probably should not be classified as chronically alcoholic. If, however, this condition had existed up to the present instead of twelve years ago, he would be chronically alcoholic according to my classification.

Another case might be that of a person who admits having been inebriated half a dozen times in his life but who has not tasted any kind of liquor in fifteen years. I believe the condition of such a patient is concealed chronic alcoholism. The pattern for addiction to alcohol,

or the likelihood of specific sensitization, is long buried in the past but can be redeveloped quickly, as in the case of a person with true chronic alcoholism.

Still further, the person who has taken alcoholic medicine at regular intervals for the relief of recurring pain and discomfort, for example, at the onset of recurring common colds or painful menstrual periods, is in my opinion a patient with concealed chronic alcoholism.

It is not my purpose to say that most of the population are afflicted with true chronic alcoholism, but rather to point out that many may be considered so, or at least potentially so, if their history approaches that set forth here as the history of the patient with true chronic alcoholism and if, in addition, they are suffering from a condition demanding even mild surgical treatment.

By this I mean to say that a great many patients are surgically treated every day who never are suspected of tolerance to alcohol or of need of it under stress, in "shock" or when undergoing operation. There are many such persons who on psychic or physical stimulation may be precipitated into the mental state of the alcoholic addict at his worst.[15] Whereas many may wish to omit completely the moral and ethical considerations with regard to true chronic alcoholism, it is essential for all physicians to try to diagnose the condition and recognize the need for prophylactic as well as active treatment when there is an accompanying surgical state. Vitamin replenishment is always advisable, especially as concerns vitamins B and C. Opinions vary about completely omitting alcohol.[16]

Any number of predisposing factors besides an imminent or an emergency surgical condition can produce a recrudescence of concealed chronic alcoholism to an obvious state of alcoholism, with only a small alcoholic intake or none at all. These include: fatigue; bad hygiene; overwork; lack of rest, recreation or sunlight; overindulgence in tobacco, coffee, tea or other nonalcoholic stimulants; indulgence in narcotics; poor heredity;[15] bad environment, emotional instability from whatever cause, and organic and functional diseases of all kinds.[17]

Physical Findings.—At the completion of the patient's history the examiner will suspect, or nearly rule out, the probability of concealed chronic alcoholism.

The objective findings of concealed chronic alcoholism include all positive data obtained from the history as related by the patient and

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15. Sereghy, E., and Marcinkievics, A.: Importance of Vital Resistance in Surgery, Orvosi hetil. **80**:815-818 (Aug. 29); 842-845 (Sept. 5) 1936. Kelly.[3] Silkworth[5a] Knight.[10] Baonville and Titica.[11d]

16. Cowles.[11a] Silkworth.[5a]

17. Carroll, F. D.: "Alcohol" Amblyopia, Pellagra, Polyneuritis: Report of Ten Cases, Arch. Ophth. **16**:919-926 (Dec.) 1936.

his relatives and as indicated by the classification just described. They also include data which can be obtained at the time of routine physical examination. In some cases the findings are limited to responses from the nervous system, obtained either by observation or by questions and answers. In other cases data are obtained by physical examination, by neurologic examination and by certain laboratory tests.

Exclusive of the results of the usual physical examination, certain evidence can be gathered which may help to classify the condition. A patient who avoids looking the examiner straight in the eye on direct questioning is to be suspected of this condition. When such avoidance occurs repeatedly, even after one becomes fairly well acquainted with the patient, it may be taken as favoring a diagnosis of alcoholism.

A patient who cannot sit still or keep his hands still, or who appears generally irritable, also presents possibly contributory indications. Other suggestive phenomena include the following, with due consideration for extenuating circumstances in the individual case: (*a*) exaggerated speech, affectation or variability of talk; (*b*) any behavior in speech, looks, talk or locomotion which seems to indicate that the patient is ill at ease; (*c*) needless repetition on the patient's part of any part of the history or conversation between him and the physician; (*d*) the inability of the patient to exhibit normal psychic, intellectual, moral and physical control during times of suggestion by the physician examining him; for example, when he shows repeated and apparently embarrassed avoidance of direct answers to subtly reintroduced questions.

Unwarranted or false cynicism which does not appear to be explained by the patient's education or known habits, or the discovery that he is in a stratum of society, financial condition or professional standing greatly out of proportion to his appearance or to his known past ability should be considered indicative.

A complete physical examination is necessary to indicate many of the objective signs of true or concealed chronic alcoholism. Many of the positive signs duplicate some of those partly diagnostic of numerous diseases of all kinds.

I shall list the positive ones as though they occurred in an otherwise normal person not suffering from any definite functional disease of the nervous system, from any metabolic disorder or from any systemic disease other than the condition requiring surgical attention.

First are the signs from an examination of the head and neck: an overanxious expression of the face; increased flushing of the skin; signs of premature age, such as gray hair and changes in the skin, deep wrinkles, cutaneous blemishes, or sometimes pallor, not explained by the other habits of the patient. Sometimes the appearance of the face entirely belies the existing condition, yet that condition can be recognized by a fleeting expression of emotion not explained by what the patient

or the examiner is doing; often a patient will look upright and serious and utter exactly contrary remarks. At other times he may look jovial, peaceful and contented while making a statement completely at variance with this facial expression. A repetition of these phenomena several times during a physical examination is sometimes of strong diagnostic significance. In the same way, otherwise unexplained emotional upsets should be taken into account.

Observation of the neck may show pulsation not borne out in other expected signs of hyperthyroidism or of circulatory or nervous disease.

Although the finding may not be altogether reliable, disproportion between the size of the neck and that of the head may be a point to consider. A patient may look as though his head did not fit on his shoulders, and no explanation is found in heredity or habit. Here a close search for the reason has revealed the condition under discussion.

This same incongruity between the features—nose, eyes, mouth, ears and hair—has been observed by me in patients of this type in whom there was no other condition to explain it.

Extremes of regularity of features and good proportion between head and neck also are seen commonly. But there is something so obviously present in the facial expression and the way the head is carried that it is possible to say that the patient has or has not good character.

There is a type of face, seen in both males and females, which conforms to no set rule, in which there appears at times or even all the time to be something that should not be there, or something not there that should be there. Some persons repel by their facial expression, as though they withdrew from the circle of others present. These same persons can consciously or unconsciously attract by some vague change in their expression. All things being equal, however, it is significant when a patient seems distant or suddenly gives some obscure sign in his facial expression that he is once more "with us" or receptive of what is said to him. Briefly, this change in facial expression or in "atmosphere" which cannot be traced to definite poses or movements can sometimes be seen to occur several times during the examination of a patient of the type described as having concealed chronic alcoholism. Some of these patients may be said to smile without really smiling or to laugh without really laughing. Others show nothing more than a strange clouding of expression, which may be only momentary but is often repeated. The gaging of these details will be difficult for an examiner who judges his patient too early, too severely or unjustly or neglects to ask for important facts.

What I have just said applies also to the patient in whom one "feels" a distinct lack of confidence. Sometimes all efforts will be futile, and

nothing the physician can do will ever establish complete "contact" with the patient. There are great differences in the powers of observation of different examiners. This is no reason to exclude admission of the fact that it is possible to observe strange, unexplained changes in facial expression on some patients, or that one may recognize incongruities not explainable on the basis of organic or functional disease.

Examination of the chest and abdomen cannot be accurately separated from that of the extremities. It is true, as well, that it is physically impossible to particularize the impression obtained from the entire body. A few suggestions may be fitting, however, regarding the chest and abdomen. Great disproportion between the size of the thorax and that of the abdomen in regard to length of the axis of the spinal cord can signify either great "strength of character" or marked "weakness." Either of these can be interpreted in the individual case to predispose toward, or to exclude, the consideration of concealed chronic alcoholism.

Failure of clinical examination to demonstrate disease of the respiratory tract does not exclude its presence. Laboratory aid must be employed. Presuming that laboratory aid is immediately available and that it is possible to exclude organic disease and cardiac instability of any kind, any change in the respiratory rate or in the pulse rate to considerably above normal may have significance. This often occurs reflexly on impulses from the central nervous system, unexplained otherwise than by chronic alcoholism. These abnormal channels are often out of reach of suggestion or of appeal to the patient to try to calm himself. I acknowledge that many possible direct and indirect factors may initiate changes in the respiratory rate and the pulse rate. One must exclude any condition except the condition requiring surgical treatment and concealed chronic alcoholism, as though all other diseases or disturbances had already been proved absent by repeated examinations, laboratory tests and lack of proof of competent cause.

Increase in the respiratory rate, if the chest (including the heart) is otherwise normal, should furnish a clue to reflex stimulation of the respiratory center from some undiscovered cause. This cause may be concealed chronic alcoholism. Obviously, exceptional care must be taken in ruling out other likely reasons, for the condition calling for surgical intervention may itself bear a close relation to a rapid pulse rate or to deep respirations.

Gross disproportion with regard to the distribution of fat in the chest and the abdomen may furnish contributory evidence. The case of the prematurely portly but otherwise normally proportioned man may be a good example. There may be a redundancy of the abdomen or other fat deposits which appear to be out of proportion to the patient's

age or endocrine makeup. When this disproportion is sensed as gross without the examiner knowing exactly why, even when there are endocrine disturbances apparently not of long standing, a connection with alcoholism may be imagined. Absolute proof may be absent. The cause of such incongruity I do not profess to know, but the recognition of it is possible, and when it is properly associated with the many other identification marks it becomes a valuable sign.

The physical characteristics of a body obviously indulged and abused are naturally altered in many ways, especially over the thorax and abdomen. Here, as elsewhere, heredity, environment, habit and use determine the particular aspect of much that can be seen on physical examination.

If the data from a study of the patient's habits, environment, development and occupation are insufficient to explain abnormal thoracic and lumbar curvatures, these departures from normal may or may not be explained on the basis of disease. When these curves appear to accompany other abnormal and inexplicable findings, the patient may be classified as potentially a victim of concealed chronic alcoholism.

Such close contiguity exists between many of these unexplained abnormalities and organic changes of hitherto explained cause that it will be difficult for me to prove my contentions.

Examination of the extremities may afford little of diagnostic evidence beyond that which is simply contributory to the already admitted variables. Again, it is believed that unusual characteristics of the arms, hands or fingers may give reason to suspect alcoholism. Sometimes a man's hands will appear soft and flabby, even with lack of care. Perhaps, the influence of environment and occupation aside, there is a relation between the firmness of the hand at the junction of the metacarpals and first phalanges and the qualities of determination, firmness, strength, regular habits and solidarity. It is probable that hereditary influences may be responsible for such firmness. This structural characteristic of the hand is best demonstrated when the examiner shakes hands with the patient and asks the patient to relax his hand. The hand may feel like flabby, inanimate meat or may be firm, inflexible, solid and nonrelaxable. When this strong hand, that is, a hand characterized by inflexibility during forced relaxation, is encountered in addition to other completely satisfactory characteristics all the way through the physical examination and history, there is little likelihood of concealed chronic alcoholism. The opposite condition of the hands, after exclusion of hereditary, developmental, occupational or environmental predispositions, may indicate concealed chronic alcoholism. It is strange also, but true, that grossly stiff, inflexible, rough hands may be particularly noticeable

in contrast to the rest of the patient's physical characteristics. Paradoxically, this finding also may suggest the diagnosis of concealed chronic alcoholism.

It is probable that truly great disproportions in the appearance of the hands, especially in texture and flexibility, length of digits, and breadth and girth, should be remembered among the details one should look for in compiling a list of unanswerable or little understood physical findings which when totaled from the entire examination may help in the diagnosis.

The same may be said of the legs, the arms and the feet. Examination of any patient completely naked makes the task slightly easier, for a person may seem much more perfectly proportioned without clothes than he does fully dressed. Another may appear almost weird, with disproportionately large hands and shriveled legs. Another may have an otherwise unexplained center of balance or pose, as he stands, which, in addition to a strangely flat region over the buttocks, seems decidedly incongruous in the presence of large shoulders and large knees and ankles. None of these characteristics is likely to be thought of in connection with alcoholism unless the examiner tries to catalogue the detailed observations and to exclude other obviously possible causes for each finding.

A few great studies have been made of races, types, figures, measurements, features and general racial physical characteristics, but not many practical specific genetic conclusions have been formulated. Certainly they are not generally appreciated. The task of bringing such a work to culmination must be almost endless. The problem under discussion is even more complex.

Let it be supposed, however, that one is able to discover in the patient several positive and otherwise unexplained incongruities, abnormalities or distortions of action, of consistency or of measurement and perspective. There should be no objection to the application of several of these positive "hints" toward the solution of a most difficult problem in diagnosis. The physician is limited only by the quality and extent, first, of his education and, second, of his powers of reasoning and ability to observe with all the senses delicately integrated. In addition, there must be a positive attempt to employ the so-called sixth sense, a higher or more refined sense than the recognized senses of touch, smell, taste, sight and hearing.

There can be no doubt that it is possible for some other sense to supersede these recognized senses, if for no other reason than that absence of one sense has sharpened one of the other remaining senses, to such an extent, for instance, that a "blind man can see." I may

refer also to the psychologic studies in extrasensory perception recently performed at Duke University.

Of course, many, if not all, physical characteristics may be the sum total of results of interplay among the endocrine glands.[12] Reason does not allow one to exclude these glands from consideration. With some training, it may be possible to remember certain outstanding endocrine markings, but the number of possibilities is unlimited because of the polymorphous heredity of human beings and the already known and numerous variables in the classification of the endocrine glands and their functions.

Further, the significance of seemingly outstanding characteristics of the patient must often be minimized in the face of stronger controversial evidence. If, for example, one should observe closely a woman who is obese and appears summarily to suffer from pituitary, ovarian and hypothyroid disease or from imbalance among the indicated glands, one may find that her body functions excellently as a whole. She may have no subjective symptoms and yet may exhibit many departures from normal. She may have been productive of children, a good mother. Her abilities as a business manager and housewife may be unexcelled. She may by nature be constantly good and even-tempered. It is best, however, to record her "faults" even though they do not seem to be associated with the slightest incongruity of physical, mental, intellectual, social or moral life. If she later undergoes operation, one may be forewarned, at any rate, even though she has never shown other findings or history suggestive of concealed chronic alcoholism.

In conclusion, it is best to "size up" the patient from the point of view of every characteristic one can determine from him before making a direct diagnosis of concealed chronic alcoholism. History, physical examination and special examination for incongruities of all types must be made. Just as some one once said that "ugly people do ugly things," so some one has said as well that "handsome is as handsome does" and that "beauty is skin deep."

From the point of view of the physical proportions and characteristics alone, it is well to try, from the recording of the history and general observations up to the end of the detailed physical examination, to correlate, as one proceeds, all the data possible, using one's powers of observation and senses as though they were a fine sieve, able to sift out what would be missed by habitual neglect of the many details mentioned.

I fully realize the need of apologizing if what has been written, all too vaguely, appears ill considered or unsoundly formulated. Perhaps some of the ideas are clouded by fogs not yet cleared away by scientific investigation and exact terminology.

CONCLUSIONS

In many surgical patients who have in the past indulged in a variable intake of alcohol there appears to be a condition often unrecognized, which I should like to call concealed chronic alcoholism.

Treatment consists in appreciating the importance of the condition early in the course of surgical treatment and in the prescription of alcohol in addition to the commonly used sedatives before dangerous depression or complications have set in. Vitamin medication is indicated preoperatively and postoperatively.

A new and arbitrary (but indicated) rule of including in the first diagnosis of the condition of the surgical patient an opinion as to the possibility that concealed chronic alcoholism (or a tendency toward alcoholism) is present would guarantee the patient a safer course during his stay in the hospital.

Much can be learned from a patient as to the possible presence of concealed chronic alcoholism by a careful recording of detailed histories, a complete physical examination and close observation for changes in physiognomy and general physical appearance; also, by a careful noting of numerous incongruities, various endocrine activities and evidences of mental and emotional instability. A brief summary of all such positive findings should be entered on each patient's chart. The surgeon should consider the possible role of alcohol in every case he observes.

SUMMARY

A vague feeling that surgeons often neglect to consider chronic alcoholism as sufficiently significant in any surgical case until the patient has nervous symptoms and depression, often bordering on mania, or other complications has prompted the recording of a surgeon's impression of what he has chosen to call concealed chronic alcoholism, a term which applies particularly to patients who are actually chronically alcoholic but whose condition often goes unrecognized.

Eight detailed histories of patients treated personally—all but 2 of whom were aided by small doses of alcohol—are included in this article.

A discussion and description of fine points in diagnosis, as well as a hint about "extrasensory perception" of symptoms of concealed chronic alcoholism, are included and offered with extreme caution as to their complete reliability.

PERIPHERAL VASCULAR STATUS OF ONE HUNDRED UNSELECTED PATIENTS WITH DIABETES

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The relation between diabetes and the occurrence of peripheral occlusive arterial disease has been the subject of a voluminous literature. It is not our purpose to review the many articles on this subject. It is sufficient to point out the existence of a number of conflicting opinions which are difficult to correlate.

There are those who hold that there is a definite causal relation between diabetes and peripheral arterial disease. Hallock[1] stated: "The diabetic state either initiates early or accelerates the development of premature arteriosclerosis in the young adult." One finds statements such as that of Ruprecht:[2] "As a general rule, regardless of the youth of the patient, a diabetes of 5 years or more duration will produce arteriosclerosis." Others consider that the increase of arterioclerosis in diabetic persons is due to neglect of diabetic treatment. Bowen,[3] on the basis of roentgenologic studies of extremities over a period of years, stated that the development of severe vascular pathologic conditions in diabetic patients requires several years of neglect of the diabetes. Joslin[4] expressed the conviction that arteriosclerosis is secondary to diabetes and that the severity of the former is in direct proportion to the duration of the latter. Allbutt[5] noted many instances of sclerotic

From the Clinic of Sympathetic and Vascular Surgery, Mount Zion Hospital.

1. Hallock, P.: Arteriosclerosis in Young Diabetics, Am. J. M. Sc. **192**:371, 1936.

2. Ruprecht, A.: Diabetes Mellitus in Its Relation to Vascular Disease, J. Oklahoma M. A. **26**:284, 1938.

3. Bowen, B. D.; Koenig, E. C., and Viele, A.: A Study of the Lower Extremities in Diabetes as Compared with Non-Diabetic States, from the Standpoint of X-Ray Findings, with Particular Reference to the Relationship of Arteriosclerosis and Diabetes, Bull. Buffalo Gen. Hosp. **2**:35, 1924. Bowen, B. D., and Koenig, E. C.: Arteriosclerosis and Diabetes Including a Roentgenological Study of the Lower Extremities, ibid. **5**:31, 1927.

4. Joslin, E. P.: Arteriosclerosis and Diabetes, Ann. Clin. Med. **5**:1061, 1927; Arteriosclerosis in Diabetes, Ann. Int. Med. **4**:54, 1930.

5. Allbutt, T. C.: Diseases of the Arteries, Including Angina Pectoris, London, Macmillan & Co., 1915, p. 280.

changes in diabetic children. Morrison and Bogan [6] found that the incidence of vascular calcification as determined by roentgenograms is higher in diabetic than in nondiabetic persons and that calcification increases with age and with the duration of diabetes. Brown [7] stated that every diabetic person over the age of 50 who has had diabetes for a few years will show arteriosclerosis of the feet on careful examination.

On the other hand, there are those who believe there is no direct relation between diabetes and vascular changes. Hekimian and Vogel,[8] reviewing autopsies on 84 diabetic persons, found no instance of death caused by arterial degenerative disease before the fourth decade; 75 per cent died after the fifth decade. Leutenegger,[9] investigating the clinical evidence of vascular change in 1,000 diabetic persons, stated that a specific diabetic arteritis does not exist, since positive evidence of such change was completely absent in those under 40; in about 50 per cent of his cases of five or more years' standing there was no clinical evidence of vascular disease, the latter occurring mainly in the sixth and seventh decades. These and other writers have advanced the opinion that improvement in the treatment of diabetes has so lengthened the life span of diabetic persons that they now live long enough to acquire coincident nondiabetic degenerative arterial disease.

In the clinic of sympathetic and vascular surgery of the Mount Zion Hospital, there is a considerable number of patients who complain of symptoms referable to disease of the peripheral arteries or who have been referred by other clinics because of subjective or objective evidence of abnormal peripheral circulation. A number of these are diabetic persons in various advanced stages of degenerative arterial disease. Impressed by the greater danger of such changes to diabetic than to nondiabetic persons, we were led to examine clinically a series of 100 unselected patients with diabetes with a view to determining their status as to peripheral vascular disease. In this investigation we sought not only the objective evidence of vascular disease but also the symptoms most commonly associated with disturbed peripheral circulation. From the accumulated data we hoped to obtain information as to any existing relation between diabetes and peripheral arterial degenerative disease and as to any relation between the severity or duration of the diabetes and the extent of such arterial degeneration. The data would furnish,

6. Morrison, L. B., and Bogan, I. K.: Calcification of the Vessels in Diabetes: Roentgenographic Study of Legs and Feet, J. A. M. A. **92**:1424 (April 27) 1929.

7. Brown, A. G., Jr.: Diseases of the Blood Vessels of the Extremities in Diabetes, South. Med. & Surg. **92**:264, 1930.

8. Hekimian, J., and Vogel, S. A.: A Study of Diabetic Deaths Based on Autopsies, New York State J. Med. **34**:385, 1934.

9. Leutenegger, F.: Klinisches Vorkommen von Gefassveränderungen bei 1,000 Diabetikern, Ztschr. f. klin. Med. **119**:165, 1932.

too, a baseline in accordance with which subsequent changes in the peripheral circulation could be more accurately gaged in future examinations.

The patients were taken at random from the metabolic clinic. This clinic is under the direction of Dr. Russel Rypins, who has made a special study of diabetes. The diabetic patients are under close scientific surveillance. In addition, each patient rotates approximately every two months through a special chiropody clinic under the care of Dr. D. Kanter, who has been specially trained in the care of diabetic feet and who is well aware of the complications incident to ill advised chiropodic treatment for these patients. Frequent consultations are held between the physicians of these two clinics. With few exceptions the patients had not previously applied to the clinic of sympathetic and vascular surgery.

Our examinations consisted in the collection of certain important data from the history, including close questioning regarding symptoms of vascular disease. (This investigation of symptoms has been somewhat neglected in reports by others.) The patient was then put through a routine examination of the peripheral vascular system. Tables 4, 5 and 6 indicate the details of the history and the examinations used in determining the status of the peripheral circulation. The examination consisted not only in estimation of the strength of the peripheral pulses but especially in a clinical determination of the vascular sufficiency or insufficiency of the extremity as a whole. Roentgen studies were not routinely made because we are convinced that they are an unreliable index of the circulatory status. Patients not infrequently have advanced occlusive degenerative arterial disease, even of the arteriosclerotic type, without roentgenologically visible calcification; others, with widespread calcification, may have extremities with a well compensated peripheral circulation. Intradermal histamine tests were not routinely done because of the variability of the effect of histamine and because of the differences in interpretation to which the tests are subject. All examinations were done by members of the staff of the clinic of sympathetic and vascular surgery, who by reason of special training and experience were well qualified to estimate the desired factors. The observations made are presented in several tables, with accompanying explanations and comments:

INTERPRETATION OF TERMS AND SYMBOLS USED IN TABLES

Severity of Diabetes:

Mild—Diabetes controlled by diet only

Moderate—Diabetes controlled by less than 15 units of insulin daily

Severe—Diabetes controlled by more than 15 units of insulin daily

Severity of Peripheral Vascular Symptoms:

Mild—Mild pains; cramps; claudication; sensory disturbances; no incapacitation

Moderate—Considerable subjective complaints; distinct claudication; patient partially incapacitated

Severe—Severe symptoms; ulceration, gangrene, amputations, marked claudication; complete incapacitation.

One or more of the foregoing symptoms determined the classification.

Severity of Findings:

Mild—Slight diminution of pulsation in one or two arteries; slight ischemia on elevation; slight rubor on dependency

Moderate—Marked diminution of pulsation in more than one artery; distinct elevation ischemia or dependent rubor, healed ulceration; changes in color

Severe—Absence of pulsation in more than one artery; very marked elevation ischemia or dependent rubor; ulceration; gangrene; amputations

Arterial Pulsations:

0—Absent
+—Barely perceptible
++—Distinctly perceptible but below normal
+++—Normally palpable.

Ischemia on Elevation
or

Rubor on Dependency:

0—Normal color
+—Slight
++—Distinct
+++—Very marked

Note that 87 per cent of the patients were over the age of 40, the greatest number being in the seventh decade. In patients under the age of 40 the incidence of severe diabetes was considerably higher than that of mild or moderate diabetes. Twenty-five per cent of the patients with severe diabetes, 7 per cent of those with moderate diabetes and 6 per cent of those with mild diabetes were under 40.

The symptoms noted are those considered most important as indicating abnormalities of the peripheral vessels. They were compiled in accordance with a scheme which proved satisfactory in the clinic of sympathetic and vascular surgery. The high percentage of various sub-

jective disorders was striking. We found that 37 per cent of patients complained of pain, 31 per cent of cramps and 38 per cent of limitation of ability to walk. Twenty-six per cent were incapacitated by conditions

TABLE 1.—*Distribution According to Severity of Diabetes*

	No. of Cases		
	Mild	Moderate	Severe
Diabetes controlled by:			
Diet only	51	..	..
Insulin, less than 15 units daily	..	14	..
Insulin, more than 15 units daily	..	..	35

TABLE 2.—*Distribution According to Sex*

Sex: Male	37
Female	63
	100

TABLE 3.—*Age Distribution in Relation to the Severity of Diabetes*

	Age									Total No.
Severity of Diabetes	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	of Cases
Mild	..	..	1	2	12	10	18	7	1	51
Moderate	..	..	1	..	1	7	3	2	..	14
Severe	..	2	3	4	9	7	9	1	..	35

TABLE 4.—*Peripheral Vascular Symptoms and Their Relation to Severity of Diabetes*

						Walking Ability (in Blocks)													
Severity of Diabetes	Pain	Numbness	Burning	Other Sensory Disturbances	Cramps	Less than 1	1-2	Up to 5	Up to 10	More than 10	Incapacitation Due to Arterial Disease	Color Changes	Inflammation	Ulcers	Varicose Veins	Gangrene	Amputations	Reaction to Heat and Cold	Total Number of Cases
Mild	17	17	6	11	19	2	1	10	8	30	11	3	2	7	20	3	1	8	51
Moderate	7	5	3	5	4	1	..	4	2	7	6	3	4	2	6	2	1	3	14
Severe	13	8	5	5	8	2	3	3	2	25	9	2	2	4	5	2	3	4	35

originating in the peripheral vascular system. We were surprised to find such a high incidence of decreased ability to walk in patients taken at random who did not consult the clinic. Pain was present in 30 per cent of 51 patients with mild diabetes and 50 per cent of 14 with moderate diabetes but in only 37 per cent of 35 with severe diabetes. Limitation of ability to walk occurred in 41 per cent of patients with mild diabetes,

43 per cent of patients with moderate diabetes and 26 per cent of patients with severe diabetes. These figures show the absence of any direct relation between the presence of symptoms and the severity of diabetes.

Of 197 lower extremities the dorsalis pedis pulse was diminished in 50 (25 per cent) and not perceptible in 21 (10.5 per cent), a total of 35.5 per cent of abnormal dorsalis pedis pulses. This pulse was impalpable in 10 per cent of the extremities of persons with mild diabetes, 18 per cent of the extremities of persons with moderate diabetes and only 9 per cent of the extremities of persons with severe diabetes. This again shows the absence of any direct relation between the severity of the diabetes and the palpability of the dorsalis pedis pulse. The high incidence of decreased dorsalis pedis pulsation is noteworthy even among

TABLE 5.—*Pulsation of the Peripheral Arteries of the Extremities*

Severity of Diabetes	A. dorsalis pedis (197 pulses)								A. tibialis posterior (197 pulses)							
	0		+		++		+++		0		+		++		+++	
	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
Mild	4	6	7	5	12	13	27	27	8	10	10	9	10	12	22	19
	1*	1*							1*	1*						
Moderate	3	2	2	2	..	2	9	8	3	4	3	2	3	3	5	5
Severe	3	3	1	..	3	3	27	28	5	6	3	3	6	5	20	21
	1*								1*							

Severity of Diabetes	A. poplitea (198 pulses)								A. femoralis (200 pulses)							
	0		+		++		+++		0		+		++		+++	
	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
Mild	2	2	1	3	9	9	30	37	..	1	1	..	2	3	48	47
Moderate	1*	..	..	1	5	3	8	10	..	..	..	..	1	1	13	13
Severe	1*	..	..	..	7	8	27	27	..	..	..	..	4	2	31	33

* Pulse missing (amputation).

patients with mild diabetes. Abnormal dorsalis pedis pulsations are rare in normal persons.

The incidence of insufficient pulsations is still higher in the posterior tibial artery, where only 92 of 197 extremities showed normal pulsations. Complete absence of pulsation was noted in 18 per cent of the extremities of persons with mild diabetes, in 25 per cent of those with moderate diabetes and in 16 per cent of those with severe diabetes. Similar relations were found in the popliteal artery, where 50 abnormal pulsations were found, and in the femoral artery, where only 15 were abnormal. It is thus clearly evident that whereas the diminution of peripheral pulsations is a common finding in unselected cases of diabetes, one can make no conclusions from the severity of the diabetes regarding the extent of changes in the peripheral pulses.

Table 6 shows the more important observations indicating the circulatory status. The degree of "elevation ischemia" and "dependent rubor" are fully given, since we consider these conditions of special value in determination of the general vascular competency of the extremity. Abnormal rubor on dependency was found in 51 per cent of mildly diabetic, 68.5 per cent of moderately diabetic, and 28.5 per cent of severely diabetic persons; abnormal ischemia on elevation was found in 34 per cent of mildly diabetic, 21.4 per cent of moderately diabetic and 7.1 per cent of severely diabetic persons. Thus again we see a relatively high percentage of vascular insufficiency in patients with mild

TABLE 6.—*Peripheral Circulatory Observations in Relation to Severity of Diabetes*

Severity of Diabetes	Rubor on Dependency							Ischemia on Elevation						Sudden Changes in Temperature	
	0	+		++		+++		0	+		++		+++		
		R	L	R	L	R	L		R	L	R	L	R	L	R	L
Mild	24	11	10	9	10	6	6	34	5	5	10	9	2	3	19	20
Moderate	3	1	2	7	7	1	1	10	2	2	..	..	1	1	3	3
Severe	23	2	3	7	5	1	2	30	2	1	1	1	..	..	7	7

Severity of Diabetes	Trophic Disturbances		Color Changes		Gangrene		Ulcerations		Varicose Veins		Sensory Disturbances		Amputations		Sclerosis of Vessels	Total Number of Cases
	R	L	R	L	R	L	R	L	R	L	R	L	R	L		
Mild	1	..	1	3	..	..	1	1	18	19	..	1	1	1	26	51
Moderate	1	..	..	..	1	..	1	..	6	5	2	1	..	1	4	14
Severe	3	3	..	..	..	..	1	..	6	6	..	..	2	..	8	35

TABLE 7.—*Associated Diseases in Relation to the Severity of Diabetes*

Severity of Diabetes	Total No. of Cases	Generalized Arteriosclerosis	Arterial Hypertension	Angina Pectoris
Mild	51	31	31	7
Moderate	14	5	5	2
Severe	35	14	13	2

diabetes and the highest degree in those with moderate diabetes, while those with severe diabetes have the lowest incidence.

Table 7 indicates the incidence of disorders of the general vascular system and their frequency in the various degrees of diabetes. There is nothing to indicate that the frequency of these disorders increases with the severity of diabetes. In fact, the highest percentage was found among the patients with mild diabetes.

It is interesting that 8 (59 per cent) of 14 patients with diabetes of less than one year's standing had definite generalized arteriosclerosis. Not one of the patients with arteriosclerosis was under the age of 51. Irrespective of age, 52 per cent of patients with diabetes of five years'

duration or less showed generalized arteriosclerosis, whereas 70 per cent of those with disease of over five years' duration displayed generalized arteriosclerosis.

TABLE 8.—*Presence of Arteriosclerosis in Relation to Duration of Diabetes*

Duration of Diabetes	Arteriosclerosis									Number of Arteriosclerotic Patients	Number of Cases
	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90		
Less than 1 year	..	..	..	..	..	2	6	..	..	8	14
1 year	..	..	..	..	..	..	1	..	..	1	2
1-2 years	..	..	..	..	1	3	..	1	..	5	7
2-3 years	..	..	..	..	..	..	1	..	..	1	9
3-5 years	..	..	..	..	1	3	4	3	..	11	18
5-10 years	..	..	..	..	..	2	6	5	..	13	29
10-15 years	..	..	..	..	..	1	4	1	..	6	9
15-20 years	..	..	..	..	..	..	2	..	..	2	6
20-30 years	..	..	..	..	..	2	..	..	1	3	5
More than 30 years	..	..	..	..	..	..	..	..	..	..	1

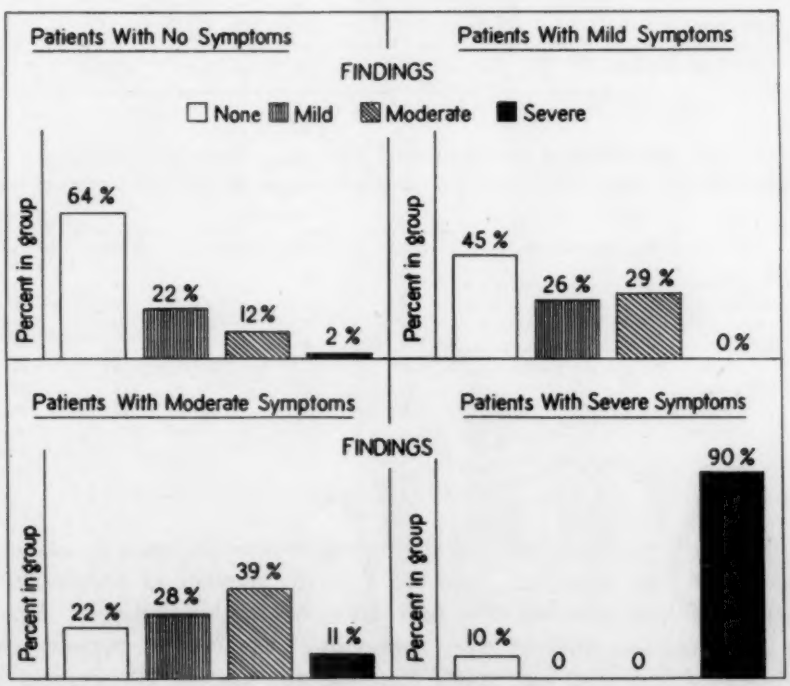

Chart 1.—Symptoms and findings in cases of mild, moderate and severe diabetes.

Although the foregoing tables show no definite relation between the degree of symptoms or of findings and the severity of the diabetes, there is a direct relation between the degree of symptoms and the objec-

tive findings. In 64 per cent of cases in which there were no symptoms there were no objective findings, whereas in 90 per cent of those with severe symptoms there were marked findings. Data on patients with mild and moderate symptoms may be noted in the chart. Thus the search for symptoms of peripheral vascular disorder, often neglected by other authors, gives a valuable clue to the presence of objective vascular abnormalities.

TABLE 9.—*Relation of Duration of Diabetes to Severity of Symptoms*

Duration of Diabetes	Symptoms				Total Number of Cases
	None	Mild	Moderate	Severe	
Less than 1 year	9	1	4	..	14
1 year	1	1	..	..	2
1-2 years	3	3	..	1	7
2-3 years	5	2	2	..	9
3-5 years	4	9	3	2	18
5-10 years	12	10	4	3	29
10-15 years	4	2	1	2	9
15-20 years	3	1	1	1	6
20-30 years	..	2	2	1	5
More than 30 years	..	..	1	..	1

TABLE 10.—*Relation of Duration of Diabetes to Severity of Findings*

Duration of Diabetes	Findings				Total Number of Cases
	None	Mild	Moderate	Severe	
Less than 1 year	7	4	3	..	14
1 year	2	..	..	..	2
1-2 years	4	2	1	..	7
2-3 years	5	3	1	..	9
3-5 years	10	3	1	4	18
5-10 years	12	7	6	4	29
10-15 years	2	1	4	2	9
15-20 years	3	..	2	1	6
20-30 years	..	2	2	1	5
More than 30 years	..	..	1	..	1

Whereas all symptoms and findings are more frequent in cases of diabetes of long standing, there are a goodly number of persons with diabetes of long standing who have no symptoms or findings. Again, we may note that findings were absent in 50 per cent of persons with diabetes of less than one year's standing and also in 50 per cent of those with diabetes of from fifteen to twenty years' standing. The relation of the duration of the diabetes to the severity of symptoms is comparable. Thus it cannot be concluded that the duration of diabetes has any relation to the severity of the peripheral vascular symptoms or findings.

Charts 2 and 3 show that in the greatest number of cases in which there were symptoms and findings of peripheral arterial disease the patients were in the age groups in which peripheral arterial disease occurs most frequently in nondiabetic persons. There were no patients with severe symptoms or severe findings below the sixth decade.

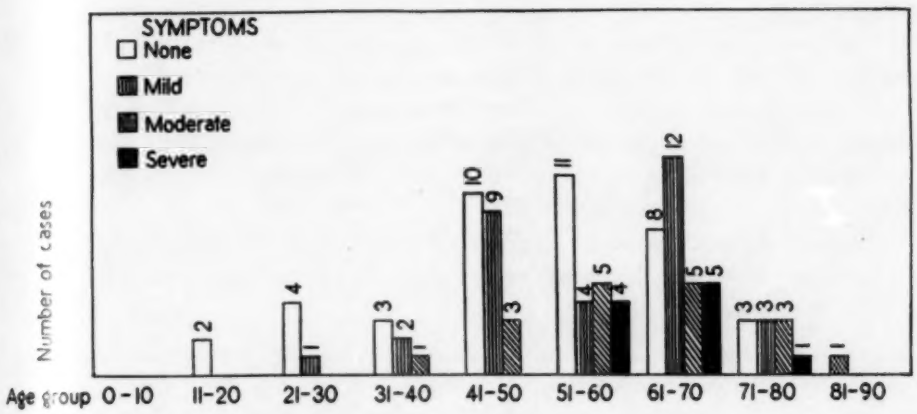

Chart 2.—Severity of symptoms correlated with age.

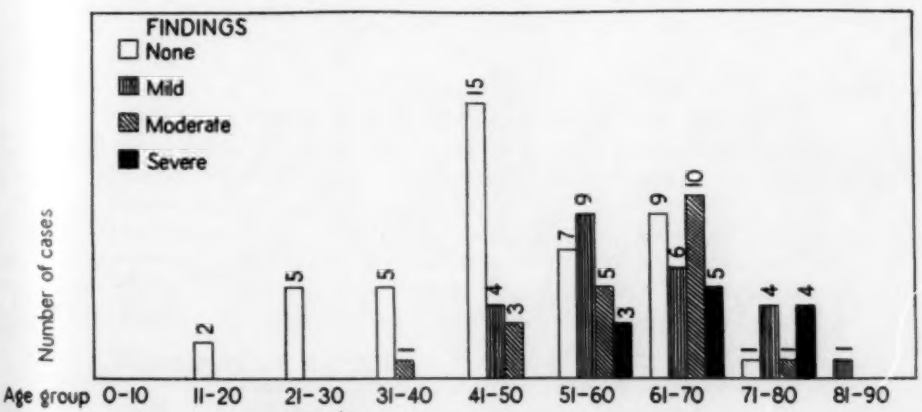

Chart 3.—Severity of findings correlated with age.

SUMMARY

One hundred diabetic persons, selected at random, were examined to determine the presence of symptoms and objective findings of peripheral arterial disease.

Over half of the patients complained of vascular symptoms. The majority showed abnormalities in the peripheral pulses and other signs of peripheral vascular derangement.

Generalized arteriosclerosis was present in 50 per cent. The greatest number of these patients were mildly diabetic persons in the older age group. The incidence of generalized arteriosclerosis showed no relation to the duration of the diabetes.

Generalized arteriosclerosis did not occur in any diabetic patient under the age of 40 and occurred in only 2 of the patients in the fifth decade.

There was no relation between the duration of diabetes and the severity of either the symptoms or findings of peripheral arterial disease.

There is a direct relation between the severity of symptoms and the severity of findings of peripheral arterial disease. The search for symptoms is important as an indication of the presence of objective evidence of peripheral arterial disease.

Findings of peripheral vascular origin were most prevalent in the age groups in which degenerative arterial disease occurs most frequently in nondiabetic persons.

CONCENTRATION OF PROCAINE IN THE CEREBROSPINAL FLUID OF THE HUMAN BEING AFTER SUBARACHNOID INJECTION

SECOND REPORT

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A. SHAPIRO, M.D.

AND

R. WARSHAW, B.A.

BROOKLYN, N. Y.

In previous communications [1] we presented data on the concentration of procaine at three levels in the cerebrospinal fluid of 122 adult patients at various times after the subarachnoid injection of 150 mg. of procaine hydrochloride in 3.5 cc. of cerebrospinal fluid.

To obtain more information regarding the factors which influence the distribution of the anesthetic in the subarachnoid space we investigated the effect of varying (1) the dose, (2) the volume and (3) the dose and the volume in the same proportion.

METHOD

Adult patients each received an injection of procaine hydrochloride, dissolved in cerebrospinal fluid, into the subarachnoid space at the interspace between the second and the third lumbar vertebra and were immediately placed in the Trendelenburg position (5 to 8 degrees).

The patients in group B received 300 mg. of procaine hydrochloride dissolved in 3.5 cc. of cerebrospinal fluid, and those in group C received 300 mg. of procaine hydrochloride dissolved in 7 cc. of cerebrospinal fluid. Samples of cerebrospinal fluid were withdrawn at different times after injection, as follows:

Group B: From 85 patients, 1 cc. at the site of injection (chart 1).
From 47 patients, 1 cc. three interspaces above the site of injection (chart 2).
From 24 patients, 2 cc. at the cisterna magna (chart 3).

Group C: From 65 patients, 1 cc. at the site of injection (chart 4).
From 53 patients, 1 cc. three interspaces above the site of injection (chart 5).
From 25 patients, 2 cc. at the cisterna magna (chart 6).

From the Crown Heights Hospital.

1. Koster, H.; Shapiro, A., and Leikensohn, A.: (*a*) Spinal Anesthesia: Procaine Concentration Changes at the Site of Injection in Subarachnoid Anesthesia, Am. J. Surg. **33**:245-248 (Aug.) 1936; (*b*) Concentration of Procaine in the Cerebrospinal Fluid of the Human Being After Subarachnoid Injection, Arch. Surg. **37**:603-608 (Oct.) 1938.

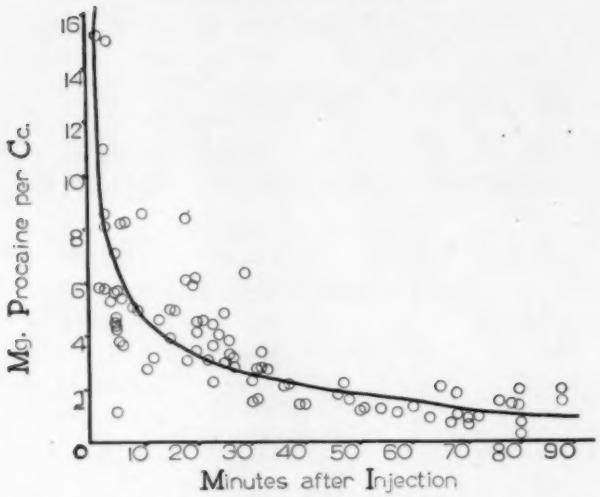

Chart 1.—Concentration of procaine in the cerebrospinal fluid at the site of injection of 300 mg. of procaine hydrochloride in 3.5 cc. of cerebrospinal fluid.

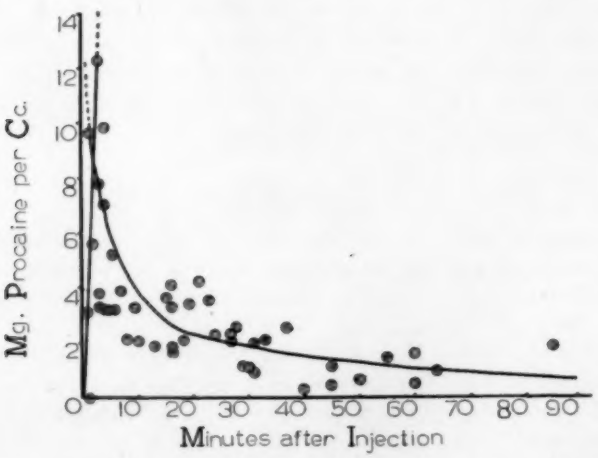

Chart 2.—Concentration of procaine in the cerebrospinal fluid three interspaces above the site of injection of 300 mg. of procaine hydrochloride in 3.5 cc. of cerebrospinal fluid.

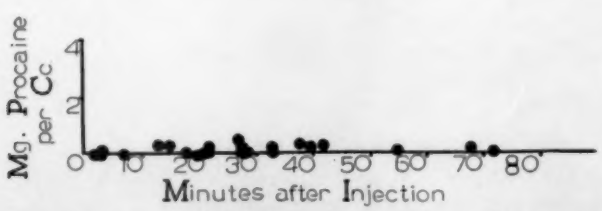

Chart 3.—Cisternal concentration of procaine in the cerebrospinal fluid after injection of 300 mg. of procaine hydrochloride in 3.5 cc. of cerebrospinal fluid.

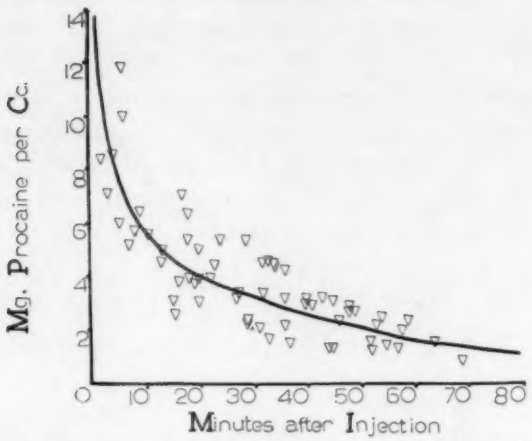

Chart 4.—Concentration of procaine in the cerebrospinal fluid at the site of injection of 300 mg. of procaine hydrochloride in 7 cc. of cerebrospinal fluid.

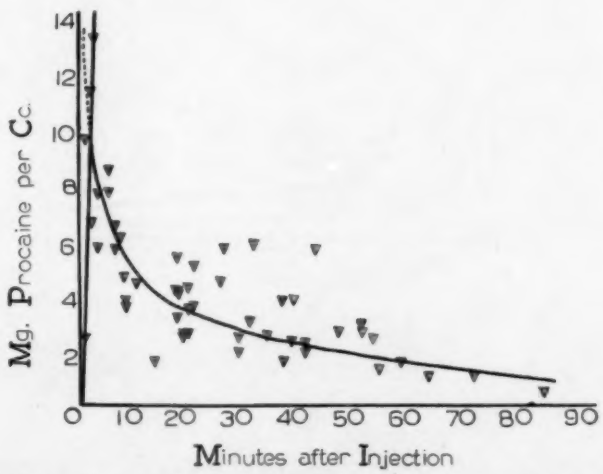

Chart 5.—Concentration of procaine in the cerebrospinal fluid three interspaces above the site of injection of 300 mg. of procaine hydrochloride in 7 cc. of cerebrospinal fluid.

Chart 6.—Cisternal concentration of procaine in the cerebrospinal fluid after injection of 300 mg. of procaine hydrochloride in 7 cc. of cerebrospinal fluid.

The concentration of procaine hydrochloride in these samples was determined in duplicate by the micromethod previously described.[2] The results are shown graphically (charts 1 to 6). Each point represents an average of duplicate.

The curves in chart 7 represent the concentration of procaine at the site of injection. It is seen that the curves are approximately the same shape. The ordinates of curve A (150 mg. of procaine hydrochloride in 3.5 cc. of cerebrospinal fluid) are approximately one-half the values of those of curve B (300 mg. of procaine hydrochloride in 3.5 cc. of cerebrospinal fluid). The ordinates of curve C (300 mg. of procaine hydrochloride in 7 cc. of cerebrospinal fluid) are similar to those of curve B but slightly above them.

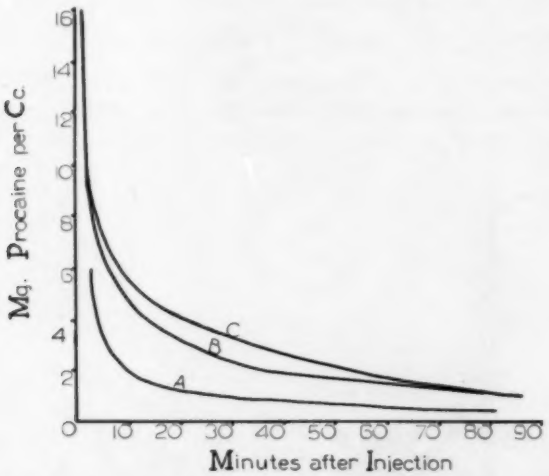

Chart 7.—Concentration of procaine in the cerebrospinal fluid at the site of injection of (*A*) 150 mg. of procaine hydrochloride in 3.5 cc. of cerebrospinal fluid, (*B*) 300 mg. of procaine hydrochloride in 3.5 cc. of cerebrospinal fluid and (*C*) 300 mg. of procaine hydrochloride in 7 cc. of cerebrospinal fluid.

The curves in chart 8 represent the concentration of procaine three interspaces above the site of injection. Here again the curves are approximately the same shape and have the same relation to each other as do the corresponding curves in chart 7.

The concentrations at the cisterna magna for 300 mg. are approximately twice the value of those obtained with 150 mg. (reported elsewhere [1b]), and the percentage of samples giving negative results is smaller.

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2. Koster, H.; Shapiro, A., and Posen, E.: A Method for the Microdetermination of Procaine in the Cerebrospinal Fluid, J. Lab. & Clin. Med. **21**:1096-1098 (July) 1936.

COMMENT

The fact that the concentration of procaine in the cerebrospinal fluid is approximately doubled when a double dose of procaine hydrochloride is injected suggests the possibility that mechanical rather than chemical factors are largely responsible for the phenomena observed. It is surprising, however, that the concentration changes so little when a double volume of cerebrospinal fluid is used to dissolve the injected anesthetic. It might be expected that the injection of 300 mg. of procaine hydrochloride dissolved in 7 cc. of cerebrospinal fluid would give concentrations lower than those following the injection of 300 mg. of procaine hydrochloride dissolved in 3.5 cc. of cerebrospinal fluid.

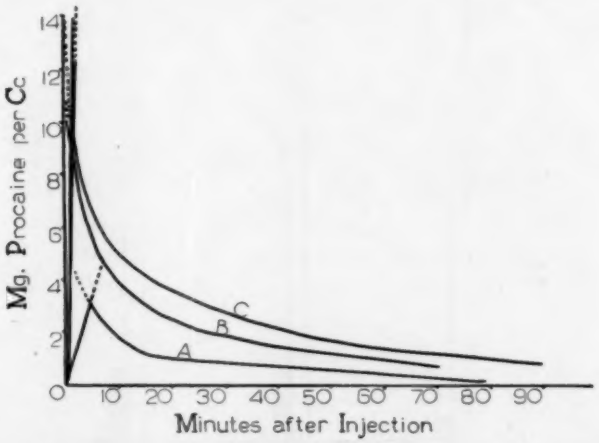

Chart 8.—Concentration of procaine in the cerebrospinal fluid three interspaces above the site of injection of (*A*) 150 mg. of procaine hydrochloride in 3.5 cc. of cerebrospinal fluid, (*B*) 300 mg. of procaine hydrochloride in 3.5 cc. of cerebrospinal fluid and (*C*) 300 mg. of procaine hydrochloride in 7 cc. of cerebrospinal fluid.

Our observations show a slight and probably insignificant difference in the opposite direction.

It is of interest to compare the maximum values found at different levels in single cases during the course of anesthesia (chart 9). These represent extreme values found in single cases and are not composite results. At the site of injection, the maximum concentration is the initial concentration and depends on the concentration of the injected solution. Three interspaces above, the highest concentration with all three types of injection was found after three minutes (chart 9) and was approximately three times as great after the 300 mg. injections as after the 150 mg. injection (4 mg., 12.3 mg. and 13.2 mg. per cubic

centimeter). At the cisterna magna the maximum concentration with the 300 mg. doses were also approximately three times that with 150 mg. (0.6 mg., 0.5 mg. and 0.2 mg. per cubic centimeter). Both in the composite curves and in the extreme values the great fall of concentration in the cephalad direction confirms our previous conclusion that the Trendelenburg posture does not cause concentrated solutions of procaine hydrochloride to flow down to the cisterna as do colored solutions in inanimate models.

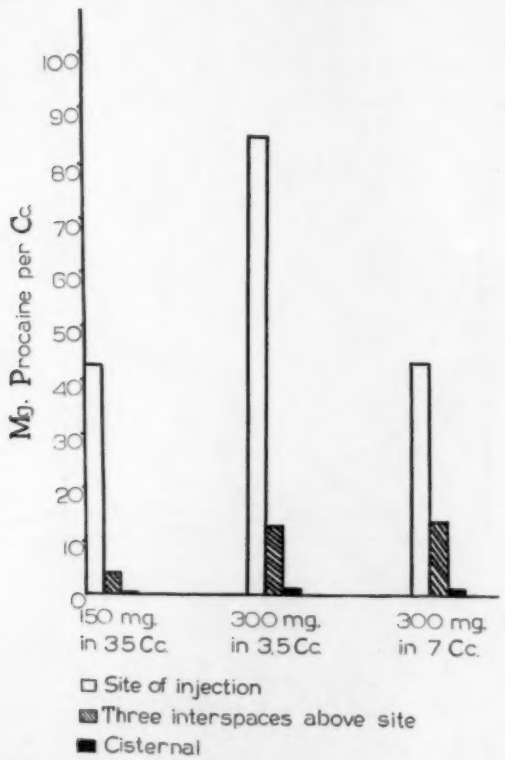

Chart 9.—Maximum concentrations of procaine in the cerebrospinal fluid.

CONCLUSIONS

The concentrations of procaine at the site of injection, three interspaces above the site of injection and at the cisterna when after injection of 300 mg. of procaine hydrochloride in 3.5 cc. of cerebrospinal fluid and 300 mg. of procaine hydrochloride in 7 cc. of cerebrospinal fluid parallel the findings previously described as occurring after the injection of 150 mg. of the anesthetic dissolved in 3.5 cc. of cerebrospinal fluid.

The injected procaine hydrochloride spreads rapidly away from the site of injection in a cephalad direction, so that the concentration of

procaine falls there and rises in the dorsal region. At no time does the concentration in the dorsal region reach as high a level as that found simultaneously in the lumbar region. When the concentration at the dorsal level has reached its maximum, it decreases at approximately the same rate as at the lumbar level and presumably for the same reasons.

Since the patients were in the Trendelenburg position from the time of injection to the time of sampling, our data do not support the assumption that the Trendelenburg position causes concentrated solutions of procaine hydrochloride to flow down to the cisterna as do colored fluids in glass models.

Doubling the amount of procaine hydrochloride injected approximately doubles the concentration found in the cerebrospinal fluid.

Doubling the volume of the injected solution causes no significant change.

MIGRAINE CAUSED BY DEMONSTRABLE PATHOLOGIC CONDITIONS

REPORT OF A CASE WITH CURE BY REMOVAL OF SMALL TUMOR IN CALCARINE FISSURE

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Whatever may be the cause of migraine, I believe the consensus is that its mechanism resides in the cerebrum and probably in the cortical vessels. The almost consistent association of the headache with fortification figures, the occurrence of which usually is the prodromal or initial event in an attack, strongly suggests that the mechanism has its beginning about the calcarine fissure.

So far as I can ascertain, no pathologic condition of the visual cortex or other structures in the brain has been found which could unequivocably be pointed out as the exciting factor in migraine. Because I feel that such a condition can be demonstrated in the case to be described, I am presenting the following report.

REPORT OF CASE

L. I.,[1] a white woman aged 30, was referred to me by Dr. C. M. Wray, of Iowa Falls, Iowa, in October 1936.

Chief Complaint.—The patient complained of headache and light flashes.

Present Illness.—Six years previously she had had her first attack of migraine. The pain was generalized in the head and was severe and throbbing. It lasted twenty-four hours and was associated with nausea and vomiting. The attack was not accompanied by flashes of light or other noticeable phenomena. After this she had frequent light attacks of headache, but one year later she had a second severe attack. The ache was referred largely to the top of the head and was made worse and more throbbing when she stooped. This attack also lasted twenty-four hours. Thereafter she suffered a hard attack associated with nausea and vomiting at least once each month, with lighter attacks in the intervals, except during a period of four months before and three months after a delivery.

She attributed the headaches to nervousness and fatigue. One year before admission to the hospital, after a hard day's work, she had had "cold and hot

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1. The case of this patient was reported from a ventriculographic standpoint in the following paper: Hyndman, O. R.: Cerebral Pneumography: Ventriculographic Interpretation of Tumors In and About Third Ventricle, Aqueduct of Sylvius and Fourth Ventricle, Arch. Surg. **36**:245-291 (Feb.) 1938.

spells." Headache was developing, for which she retired at 4 p. m. The next morning she "awoke in the hospital." At 6 p. m. her sister-in-law had found her talking irrationally, with a high fever (?). She was discharged from the hospital in twenty-four hours. She walked home, although her head was aching severely. The next day she was well, and she remained so until the delivery of a child, four months later.

Three months after the delivery the severe headaches associated with nausea and vomiting began again and occurred at intervals of two weeks to a month until the time of admission. They came on at any time during the day or night. At times she would retire feeling well and be awakened by a severe attack.

Ordinary methods of treatment, including rest and cold applications, were of no avail. Only hypodermic injections of morphine gave any relief.

About one month before her admission to the hospital she had a seizure of varicolored light flashes in the left visual field, "as if some one were waving red and green lanterns over her left shoulder." These seizures lasted from two to four minutes and at times recurred at half-hour intervals. During the seizures

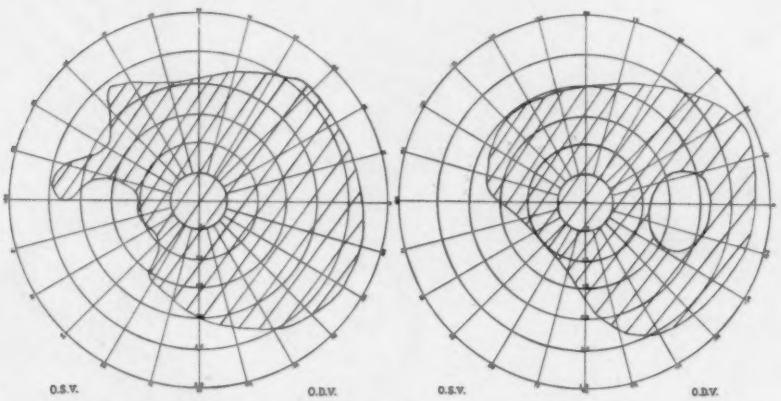

Fig. 1.—Visual fields, showing a defect in the left homonymous fields.

there were transitory weakness of the left arm and leg and lack of control of these extremities. Her husband stated that at such times she "handled her left leg like a high-stepping horse."

She stated that there was no association between the headaches and the visual phenomena.

The family history was relevant only in the fact that none of the patient's relatives had been subject to migraine or had had any condition similar to her present illness.

Examination.—General examination gave essentially negative results. The patient was obese and cheerful. The temperature was 98.2 F., the pulse rate 88 and the blood pressure 110 systolic and 70 diastolic.

Neurologic study, including examination of the ocular fundi, gave essentially negative results except for evidence of left homonymous hemianopia by gross tests. The visual fields are shown in figure 1.

Laboratory Examination.—Studies of the urine and of the blood revealed normal conditions. The Wassermann reaction was negative. The spinal fluid pressure was within normal limits.

Roentgen Examination.—A plain roentgenogram of the skull revealed a small diffuse area of calcification in the left parietal region. It was about 1 cm. from the skull and measured about 1.5 cm. in diameter.

Ventriculographic Examination.—A ventriculogram was made and proved to be normal in every respect.

Fig. 2.—Low power photomicrograph showing the tumor in cross section.

Operation.—On October 6 the right occipital lobe was explored. The cortex of the brain appeared normal in every respect. There were none of the signs of increased intracranial pressure. The occipital lobe was inspected mesially, but nothing unusual could be seen. In view of the history and visual fields, however, amputation of the right occipital pole, including the calcarine fissure, was felt to be justified. The plane of excision was made about 1½ inches (3.7 cm.) anterior to the posterior tip of the occipital pole.

Pathologic Observations.—On examination of the specimen a tumor about 1 cm. in diameter could be seen directly embedded in the region of the calcarine fissure. (This growth is shown in figure 7 of the previous report.[1]) Microscopically the tumor proved to be a hemangioma, with evidence of recent and old hemorrhage (fig. 2).

Course.—The patient recovered, and to the time of writing (two years) she has been free from headache, light flashes and seizures of transient weakness in the left arm and leg.

COMMENT

Although it might be questioned that this patient presented a typical migraine syndrome, she nevertheless presented the major elements of that syndrome. The important feature of the case is the fact that there were frequent seizures of severe migrainous headache associated with nausea and vomiting and relieved only by morphine but responding promptly to removal of the pathologic tissue. So far as is known, the patient at no time had increased intracranial pressure and the ventriculogram was normal in every respect. It seems clear that the lesion removed was the factor responsible for the headaches. The tumor itself was in the region of the right calcarine fissure and did not involve the dura. It seems fair to assume, therefore, that this is a case of an organic lesion causing attacks of migrainous headache through the same mechanism that is responsible for "idiopathic migraine" and that it provides additional evidence that this mechanism operates within the limits of the cerebrum, including its vessels and the leptomeninges.

OSSEOUS CHANGES ASSOCIATED WITH LYMPHOGRANULOMA VENEREUM

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AND
MYRA LOGAN, M.D.
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Reports of cases in which articular changes are associated with lymphogranuloma are infrequent, and reports of the association of osseous lesions with this condition are rare. Many writers have mentioned arthritic symptoms as one of the early acute manifestations of the disease. Frei [1] stated that "rheumatoid symptoms, sometimes with joint swelling" are present, and he offered the fact as evidence of the constitutional nature of the malady. Hellerström [2] noted polyarthritic symptoms in 3 of his cases. A complete report was made by Reichle and Connor [3] of a case in which there was involvement of the hip joint; this is the only report of such involvement we were able to find in the American literature. We have been impressed by the paucity of detailed case reports describing osseous and articular changes associated with lymphogranuloma and also by the fact that the data revealed by study of the records seemed to be incomplete and inadequate for critical scientific appraisal. It seemed, therefore, important to review the literature and to report 3 personally observed cases of osseous changes occurring late in the disease.

REVIEW OF LITERATURE

Koppel,[4] in 1927, reported the case of a 28 year old woman who was admitted to the hospital because of a painful swelling in the right inguinal region. The right inguinal lymph nodes were fluctuant. The right wrist and the left ankle joint were swollen. The left wrist and the right

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From the Surgical Service of the Harlem Hospital, Louis T. Wright, Director.

1. Frei, W.: Venereal Lymphogranuloma, J. A. M. A. **110**:1653 (May 14) 1938.

2. Hellerström, S.: A Contribution to the Knowledge of Lymphogranuloma Inguinale, Acta dermat.-venereol., 1929, supp. 1, p. 5; cited by Alley, R. C.: Rectal Stricture: Relation to Lymphopathia Venerea, Tr. Am. Proct. Soc. **35**:150, 1934.

3. Reichle, H. S., and Connor, W. H.: Lymphogranuloma Inguinale: Report of a Case with Involvement of the Retroperitoneal Lymph Nodes and Probable Involvement of the Hip Joint, Adrenals and Kidneys, with Autopsy, Arch. Dermat. & Syph. **32**:196 (Aug.) 1935.

4. Koppel, A.: Lymphogranuloma Inguinale, mit akuten rheumatischen Erscheinungen, Klin. Wchnschr. **6**:2469, 1927.

ankle swelled later. Erythema nodosum then developed, with lesions on both legs and elsewhere on the body. The history included syphilitic infection; five courses of antisyphilitic treatments had been given. At the time of admission both the Wassermann and the Frei reaction were positive. The patient had fever during her two weeks' stay in the hospital, but before her discharge the erythema nodosum and the articular symptoms had disappeared and the temperature had become normal. No roentgen studies were made, and serologic data were not reported.

Frauchiger [5] reported 2 cases. The patient in the first was a 48 year old woman who entered the hospital in 1933, complaining of stiffness of the right ankle, swelling of the left ankle and pain and swelling in both hands. In 1916 her husband had had a urethral discharge, swelling of the inguinal lymph nodes on the right, and pain in the right hip. Later in the same year the patient had had an ectopic pregnancy and a Bartholin abscess. In 1918 she had pain in both ankles. In 1923 she had a rectal discharge and in 1928 a rectal abscess. Rectal stenosis followed the abscess, and a colostomy was performed. Physical examination on admission showed thickened, tender elbow joints, with limitation of articular motion. The left ankle was swollen, but there was no pain on motion. Roentgen examination of the chest and Mantoux tests gave negative results. Roentgen examination of the joints showed porotic changes and atrophy from disuse of the knee joints, which were thickened and contained fluid. There was thickening of the lateral sides of the capitellum radii, with thickening of the lateral portion of the joint capsules and periostitis of the lateral surface of the radiuses.

Frauchiger's second case was that of a 33 year old man who entered the hospital in 1933, complaining of pain in the right wrist joint. He stated that he had practiced sodomy in 1924 and that this practice was followed by abscesses of the inguinal glands. His Wassermann reaction was positive at that time, and he was given antisyphilitic therapy. Rectal stenosis developed. Later he was operated on for a hernia, and subsequent to this a colostomy was performed. After the colostomy there was severe pain in the back and pain and swelling were observed in both ankle joints. In 1933, motion of the right wrist caused pain, and the wrist was somewhat stiff. There was swelling on the volar surface. The Frei reaction was positive. Results of Wassermann tests and complement fixation tests for gonorrhea were doubtful. A few days later a para-articular abscess developed and was incised. The pus was greenish yellow and odorless. It contained leukocytes but no bacteria. Injection of this pus into laboratory animals showed no tubercle bacilli. No mention was made of roentgen study.

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5. Frauchiger, E.: Polyarthritis lymphogranulomatosa inguinalis tarda, Schweiz. med. Wchnschr. **63**:1207, 1933.

Reichle and Connor reported the case of a 31 year old Negro first seen in January 1932. He complained of pain in the right groin, which interfered with walking and became severe on extension of the thigh. Two months previously he had had a urethral discharge for fifteen days. Three weeks later he had noticed swelling in the right inguinal region, followed by spontaneous rupture of the mass and discharge of a large amount of pus. The right inguinal glands were enlarged on admission. The Frei reaction was positive. The Wassermann reaction varied from negative to 3 plus on different occasions. The patient was given seventeen intravenous doses of typhoid vaccine, which was administered bi-weekly. After this he received four intravenous injections of 1 per cent antimony and potassium tartrate. Suppuration of the nodes continued. On March 17 complete resection of the right inguinal nodes was done. Postoperatively the temperature varied between 98.6 and 104 F. Pain in the right hip continued, but a roentgenogram of the joint at this time was normal. The upper end of the surgical wound was infected and discharged pus. A roentgenogram of the hip joint one month later showed a destructive process. Arthrotomy performed on April 23 released pus from the joint and revealed eroded articular cartilage. The wound was drained, and the leg was fixed in extension. The patient died on May 20. At autopsy the right hip joint contained a small amount of dark fluid, and the articular surfaces of the acetabulum and the head of the femur were roughened and discolored. The sinus observed in the right inguinal region extended into the right hip joint. The lymphatic chain from the inguinal region extended along the retroperitoneal nodes to the diaphragm, and the nodes showed the typical lesions of lymphogranuloma. This case was more thoroughly studied than any of the other cases in the literature.

Carrasco [6] examined a 22 year old man in December 1934 for bilateral enlargement of the inguinal nodes. Antisyphilitic treatment had been given, and the Wassermann reaction was negative. On two occasions the Frei test gave a markedly positive reaction, progressing even to necrosis. There was pain in the right hip joint, and extension of the leg was painful. A fresh mass of enlarged glands developed in the right iliac fossa. After about ten days the arthritis disappeared and the patient returned to work. No roentgen examination was reported. Carrasco's second case was that of a 24 year old man seen in January 1935. There was bilateral enlargement of the inguinal nodes, with marked adenopathy in the right iliac fossa and pains in the right leg. The Frei test gave a markedly positive result on two occasions. In March 1935 the patient was obliged to stay in bed because of sharp

6. Carrasco, C.: Maladie de Nicolas-Favre avec arthrite de la hanche, Bull. Soc. franç de dermat. et syph. **43**:1556, 1936.

pains in the right hip. Two weeks later the arthritis disappeared. No roentgen studies were reported.

Sézary and Saliembiez [7] reported 1 case. They examined a 31 year old woman who complained of pain in the knee joint in March 1936. She had had syphilis in 1932, bartholinitis in 1933 and an inguinal bubo resembling lymphogranuloma venereum in 1933. The inguinal bubo did not heal until April 1934. The Frei test at this time gave a positive result. A rectal stricture developed in January 1934. An iliac anus was created in October 1934. There had been two previous attacks of hydrarthrosis, in November 1934 and April 1935. Fluid withdrawn from the knee in March 1936 was injected into three different kinds of laboratory animals, but the results were not illuminating. A Frei antigen made from the fluid produced a positive intradermal reaction in the patient and in other patients known to be suffering from lymphogranuloma venereum, but the patient's serum had no such power. Injections of anthiomaline (the lithium salt of stibiothiomalic acid) were credited with curing the hydrarthrosis. No roentgen studies were reported.

Midana [8] reported the case of a 34 year old man who complained of pain in the right coxa-femur joint and enlarged nodes in the right inguinal region. An enlarged inguinal node had developed three months previously, but its incision had caused only temporary relief. Examination showed enlargement of the deep iliac glands. A diagnosis of inguinal poradenitis was made and was confirmed by the Frei test. Roentgen study showed no osseous lesions in the head of the femur or the acetabular bones, but the articular "interlinea" was "opacified." Midana stated that treatment with antimonial preparations cured (clinically) the adenopathy and the articular lesions in a little over three weeks.

Summary of the Literature.—Koppel's patient had both syphilis and lymphogranuloma. The differential diagnosis in this case was incomplete. This, with the absence of roentgen studies, makes us classify it as a case in which the picture was only suggestive of osseous changes. In Frauchiger's first case definite osseous changes were seen on roentgen examination. His second case was one of syphilis and lymphogranuloma, with tuberculosis ruled out. His failure to rule out gonorrhea and to make roentgen studies makes it unacceptable. In the case reported by Reichle and Connor, although syphilis was associated with lymphogranuloma, the articular changes found were so closely related to the suppurating inguinal glands (which did not respond to thorough

7. Sézary, A., and Saliembiez, M.: Hydarthrose récidivante et maladie de Nicolas-Favre, Bull. Soc. franç. de dermat. et syph. **43**:1573, 1936.

8. Midana, A.: Artrite dell' anca di origine poroadenitica, Minerva med. **1**: 434, 1937.

antisyphilitic treatment) that in the light of our present knowledge we believe the articular lesion to have been due to lymphogranuloma. In Carrasco's 2 cases, which were instances of lymphogranuloma, the diagnosis of arthritis was based simply on pain in the joints. Because of lack of roentgen examination and insufficient data, the diagnosis must be considered presumptive. The case reported by Sézary and Salembiez proved to be one of hydrarthrosis in a woman with syphilis, gonorrhea and lymphogranuloma. The reactions obtained with the joint fluid antigen adds weight to the evidence that the pathologic condition of the joints was due to the lymphogranuloma virus. In Midana's case slight changes were observed in roentgen examination, but we doubt that any serious bone lesion would heal so rapidly.

Since there are so few proved cases of osseous and articular lesions reported in the literature, it seems desirable to outline certain minimal standard requirements that should be fulfilled before a diagnosis is made. We suggest the following diagnostic criteria:

1. The clinical symptoms should be those of lymphogranuloma venereum.

2. The Frei reaction should be positive.

3. Pathologic, bacteriologic, serologic and roentgen studies must rule out tuberculosis, syphilis, gonorrhea, malignant tumors and pyogenic infections.

4. Definite changes in bones or joints should be evident roentgenographically.

It is only by the use of such rigid standards that one is able to differentiate many cases in which there are signs and symptoms simulating osseous or articular changes due to lymphogranuloma from the few cases in which the manifestations are undeniably due to this disease.

It should be pointed out again how rarely pathologic conditions of the bones occurring in the late stages of this condition are encountered. Hartmann,[9] of Paris, in a painstaking and intensive study of rectal stenosis over a period of forty years, has not recorded in any of his many carefully detailed case histories a single instance of involvement of the bones. In a further study of this point we have examined roentgenographically 25 patients with rectal strictures with positive Frei tests. The pelvis, hip joints and lumbar vertebrae were found to be normal.

REPORT OF CASES

CASE 1.—V. G., a Negress aged 29, was admitted to the Harlem Hospital in December 1935, complaining of pain in the right groin, which had been present for two months. She had noticed a swelling in the area of the right femoral

9. Hartmann, H.: Rectites stenosantes, in Chirurgie du rectum, Paris, Masson & Cie, 1931, pp. 166-239.

canal tw[illegible]s prior to admission. Physical examination showed her to be well devel[illegible] well nourished. The abdomen on palpation disclosed a mass in the right i[illegible]rant and tenderness over McBurney's point. Another mass, about the size [illegible] was present in the area of the femoral canal, just below Poupart's liga[illegible]s fluctuant and freely movable. Bimanual examination revealed a mass wi[illegible]ught to be a fibromyoma of the uterus, and the uterus was retroverted an[illegible]. The pulse rate and the temperature were normal. The blood pre[illegible] and 90 diastolic. The urine was normal. The white cell cou[illegible] 400 per cubic millimeter, with 69 per cent polymorphonuclear [illegible]ell count was 5,800,000 per cubic millimeter, with hemoglobin 80 pe[illegible].

A roentgenogram of the chest was normal, [illegible]. Kahn test of the blood gave a negative result. At operation the findings w[illegible] a cyst of the right ovary, a retroverted uterus in descensu and a subacutely inflamed appendix with numerous adhesions. The ovarian cyst and the appendix were removed, and the uterus was suspended by the anterior suspension method of Coffey. An incision was then made over the femoral mass, which proved to be a well encapsulated abscess over Scarpa's triangle. It contained about 1 ounce (30 cc.) of thick, yellow odorless pus. A small piece of the abscess wall was removed for study, and the cavity was packed with iodoform gauze. The pathologist reported that the tissue showed giant cells, with areas of necrosis, surrounded by epithelial cells in palisade arrangement. He made a diagnosis of lymphogranuloma.

The postoperative course was quiet. The midline incision (used for the intra-abdominal work) healed throughout its upper portion by primary intention. By the fourteenth day, a globular fluctuant mass the size of an orange had developed at the lower angle of the wound. This was incised, and 2 ounces (60 cc.) of odorless, watery pus was obtained. The patient was later discharged, with two draining sinuses—the unhealed abscess and the incised mass at the lower angle of the wound. Her general condition was good.

She was closely watched until November 1937. In spite of the negative Kahn reaction she was given antisyphilitic treatments. No improvement was seen. During this time walking became more painful, and the sinuses did not heal. She was then readmitted to the hospital. Except for the sinuses, physical examination gave negative results. The temperature and the pulse rate were normal. The blood pressure was 120 systolic and 80 diastolic.

The blood count showed 7,200 white blood cells per cubic millimeter, with 70 per cent polymorphonuclears. There were 4,700,000 red blood cells per cubic millimeter, with a hemoglobin content of 70 per cent. The Frei test with human bubo antigen gave a positive result. Roentgenograms of the pelvis showed destruction of the intercartilaginous lamina and the pubic bone (fig. 1*A*). At operation each of the sinus tracts was probed and a free piece of cancellous bone was removed. The tract was completely excised with a Bovie knife. The free wound was closed without drainage. The excised tracts granulated to some extent, but there was no primary union. The patient was discharged on the sixteenth postoperative day, with some drainage from both tracts still present.

The pathologist reported that the specimen from one of the tracts showed only dead cancellous bone.

The patient's subsequent course has [illegible]en observed. At the time of writing she is still having drainage from the si[illegible] A roentgenogram taken in December

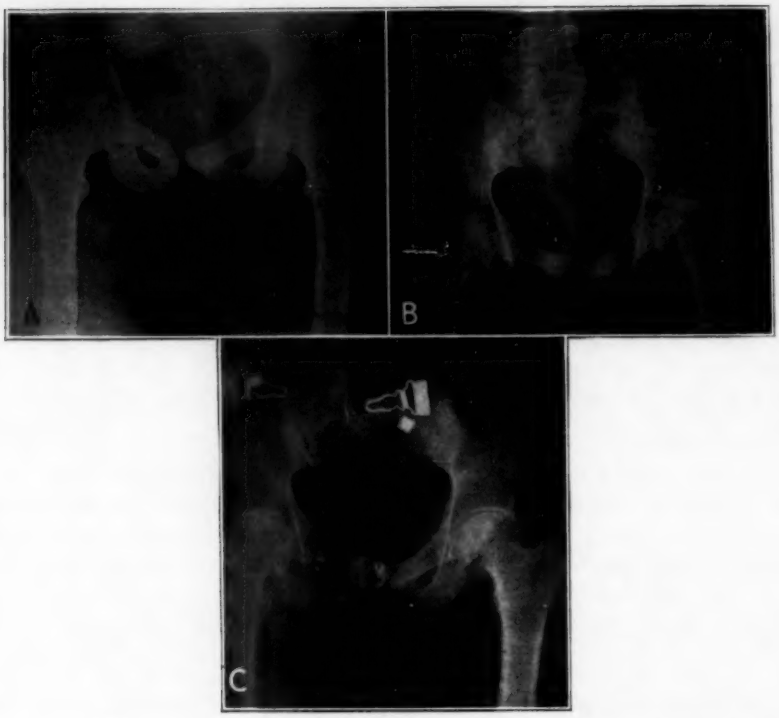

Fig. 1 (case 1).—*A*, roentgenogram taken Nov. 28, 1937, showing necrosis of bone at the symphysis pubis. *B*, roentgenogram taken June 20, 1938. The process shows progressive destruction of the pubic bones. *C*, injection of the abdominal sinus with iodized poppyseed oil.

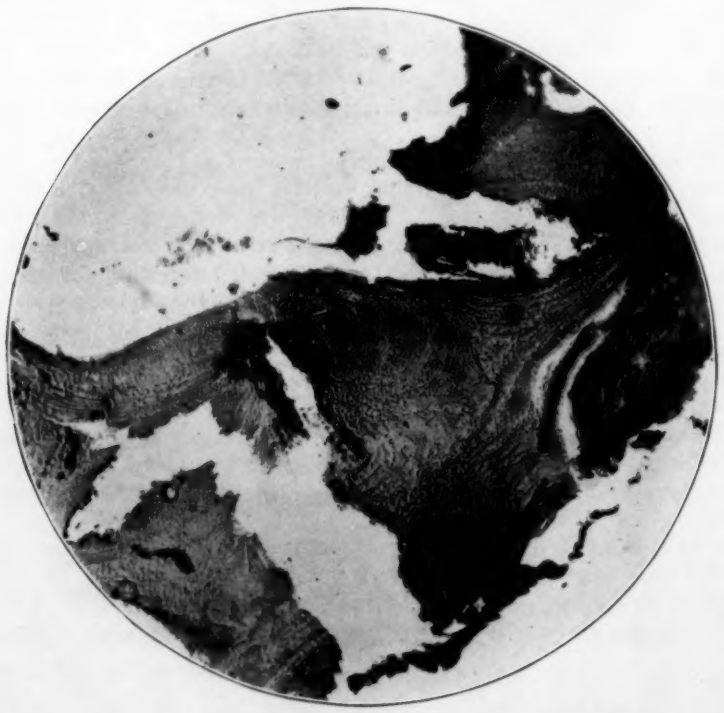

Fig. 2 (case 1).—Photomicrograph of bone removed from the sinus tract. Several pieces have been spontaneously extruded.

1937 showed increase in the destructive process in the pubis. In February the process had spread more on the right side. Comparison of plates taken in June 1938 (fig. 1 *B*) and those taken in December 1937 shows the rapid progress of the destructive process. The Frei test was repeated in July 1938, with a markedly positive result. A roentgenogram taken on Sept. 22, 1938 showed marked sclerosis in the region of both sacroiliac articulations. This was more marked on the left. There was no gross change in the process at the symphysis. A photograph taken on November 1 shows the appearance of the sinuses (fig. 3).

Injection of iodized poppyseed oil into the orifice of the sinus of the abdominal wall showed the oil to escape from the inguinal sinus, indicating a free communication between the two sinuses and the pubic area (fig. 1 *C*).

CASE 2.—I. G., a 39 year old housewife, was admitted to the Harlem Hospital on June 28, 1938. Her complaints were difficulty in walking and weakness of the right leg. Pain had been present in the right hip joint and in the lower

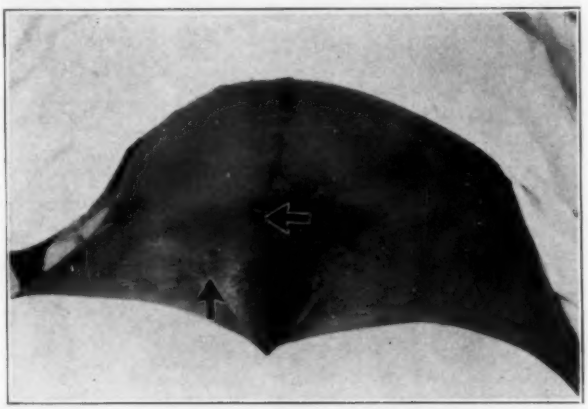

Fig. 3 (case 1).—Position of the sinuses as they appeared on Nov. 1, 1938.

part of the back for three months prior to admission. This pain had been constant but had not prevented walking.

Her history included four previous admissions to the hospital. She dated her complaints from a hemorrhoidectomy done in 1926. After this operation she had sometimes been incontinent and had sometimes had pain on defecation. In 1930 she had had her only pregnancy, which terminated in a spontaneous abortion at three months. Thick, odorous discharges from the rectum and vagina appeared in 1932. In January 1935, because of these discharges she was first admitted to the hospital.

Physical examination showed the patient to be poorly nourished. A rectal stricture which admitted only one finger was the only pathologic physical finding. The Kahn reaction of the blood was negative. The hemoglobin content was 70 per cent, and there were 4,000,000 red blood cells per cubic millimeter. The blood pressure was 98 systolic and 74 diastolic. The blood chemistry was within normal limits. A roentgenogram of the chest was normal. A colostomy was done, the proximal end of the sigmoid being used. An operative note stated that the area of rectal induration was thought to extend 7.5 cm. above the pelvic diaphragm.

The patient's convalescence was uneventful, and she was discharged on February 18. Rectal resection was done on October 23, and at the same time a new anus was constructed. The pathologist reported that the rectal tissue showed "acute and chronic inflammation." The patient was again discharged. In September 1936, the colostomy opening was closed, with no subsequent morbidity. An incisional hernia developed and was repaired in December.

Physical examination in June 1937 showed the patient to be moderately well nourished. She was continent, and the stools were of normal size. A draining sinus was present on the mesial aspect of the left buttock. Physical examination disclosed no other abnormal signs. A Frei test with human antigen gave a markedly positive reaction. The Kahn reaction of the blood was negative and urinalysis showed no abnormalities. Roentgen examination showed destruction of the medial portions of the pubic rami (fig. 4).

Fig. 4 (case 2).—Destruction of the medial portions of the pubic rami. This lesion seemed to heal spontaneously.

Comment on Cases 1 and 2.—These 2 cases fulfil the necessary requirements for a diagnosis of osseous changes due to lymphogranuloma venereum. The title of this paper was chosen because we have no desire to assert positively that the virus of lymphogranuloma venereum is the etiologic agent in the bone disease. On the other hand, the evidence for this relation seems to us to be strong. Tedder [10] showed that when the involved lymph glands are surgically removed, there is an enormous amount of periglandular exudate. In case 1 biopsy disclosed the classic picture of the disease. The material was removed from the depth of the sinus, immediately adjacent to the necrotic bone. The fact that

10. Tedder, J. W.: New Orleans M. & S. J. **90**:13, 1937.

osteomyelitis may be caused by infection of the adjacent soft tissue is not new. On the other hand, the infection may have been borne directly into the bone by the lymphatics. The occurrence of pubic necrosis in both cases may easily be explained on the basis of the lymphatic distribution. Nesselrod's [11] recent study showed that "in the female the lymphatic drainage from the external genitalia is inguinal, as in the male, but the drainage from the vagina and from the cervix is pelvic." It is generally agreed that in 90 per cent of cases of lymphogranuloma venereum in females the original infection is cervical or occurs in the posterior portion of the vagina, and rectal stricture results, the lymphatic drainage being posteriorly. The patient in case 1, we think, had the initial lesion on the clitoris or the external part of the vulva (upper margin of the labia). A massive infection spreading both anteriorly and posteriorly must be postulated for the second case, in which there were a rectal stricture and a pubic lesion. Martin [12] stated that in his experience 90 per cent of females are afflicted with rectal stricture while only 10 per cent have involvement of the genitalia and the inguinal glands. For males these figures may be reversed, but in either sex both may exist simultaneously. This is true in our experience. We have gone to great pains to eliminate other possible etiologic factors, and it is our belief that these 2 cases represent definite bone changes due to lymphogranuloma.

CASE 3.—W. W., a 53 year old Negress, was admitted to the Harlem Hospital on July 8, 1938, complaining of pain in the lumbar portion of the spine and in both hip joints, which had been present for one year. For six months prior to admission it had been more severe; it was worse on motion, in dry weather and during the day. It was relieved by salicylates. She had been taking codeine in doses of unknown size for relief of the pain. There had been nodules on the inner aspect of the right thigh and just below the jaws. These had disappeared before admission. Her past history showed that at the age of 23 the cervical lymph nodes on the left were removed because of chronic enlargement. In 1923 a colostomy was done in the New York Hospital because of rectal stricture. Antisyphilitic treatments were begun at that time. In May of that year a retrovaginal fistula developed, which was excised at the same institution. The rectal stricture was then dilated. In the three subsequent years three abscesses developed around the colostomy opening; these were opened. In 1930 the patient again entered the New York Hospital, where a cecostomy was done. Between 1921 and 1929, antisyphilitic treatment was given at intervals. In 1932 a discharging sinus developed over the sternum and one over the tenth dorsal vertebra, in addition to generalized adenopathy. In spite of the now negative Wassermann and Kahn reactions, a diagnosis of tertiary syphilis was made because of the sinuses. She was treated with a bismuth compound and sodium thiosulfate. The patient was admitted to the Harlem Hospital in 1936, for the first time (fig. 5). There was an ulcer

11. Nesselrod, J. P.: Demonstration of Genito-Ano-Rectal Lymphatics, Tr. Am. Proct. Soc. **36**:85, 1935.

12. Martin, C.: The Variety and Distribution of Gross Lesions in Lymphopathia Venerea, Tr. Am. Proct. Soc. **37**:72, 1936.

of the soft tissues over the sternum and necrosis of the bone under it. There was an area of erythema around the ulcer, which varied from 3 to 5 cm. in depth. The colostomy opening, which evidently had been made in the transverse colon, had contracted to the size of a lead pencil. The liver and spleen were palpable. A roentgenogram of the sternum showed destruction above the junction of the

Fig. 5 (case 3).—Lesion over the sternum as it appeared June 10, 1936. Note the operative scars and the hernia, indicative of multiple colostomies for a rectal stricture.

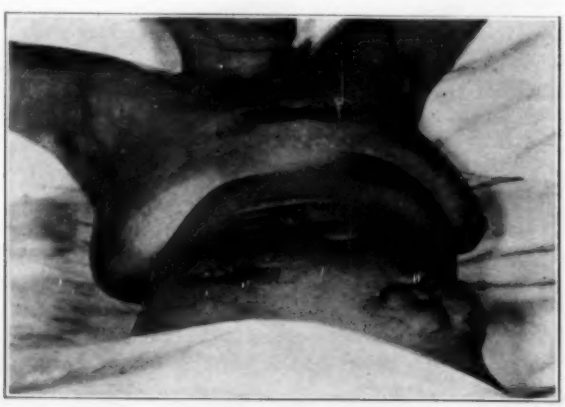

Fig. 6 (case 3).—Photograph taken on July 12, 1938. The sternal lesion is still present.

manubrium and the body of the sternum. The Kahn test of the blood gave a negative result.

Bacteriologic examination of the fluid from the sinuses over the sternum and those of the back did not reveal tubercle bacilli or actinomycetes. The blood pressure was 116 systolic and 78 diastolic. The blood count showed 7,500 white

cells per cubic millimeter, with 67 per cent polymorphonuclears and 33 per cent lymphocytes. There were 4,010,000 red blood cells per cubic millimeter and a hemoglobin content of 60 per cent. Urinalysis showed a specific gravity of 1.012, a 2 plus reaction for albumin, granular and hyaline casts, white blood cells and urates. The temperature on admission was 98.2 F., and the pulse rate was 84. The temperature rose at intervals during the patient's stay in the hospital to 100.8 F. Specimens of the soft tissue and of the bone from the ulcer showed, on pathologic examination, a chronic inflammatory process.

Physical examination in 1938 showed the patient to be poorly nourished. The mucous membranes were pale. The abdomen showed cecostomy and colostomy scars and two draining sinuses. The sternal sinus was still present (figs. 5 and 6). There were marked kyphosis and moderate scoliosis. A roentgenogram of the pelvis was normal. The dorsal portion of the spine showed fusion of the fourth and fifth and of the tenth and eleventh thoracic vertebrae, with destruction of the intervertebral disks and compression of the tenth and eleventh vertebral bodies. Examination of the chest gave negative results, but the spinal lesion seemed to be tuberculous.

Comment on Case 3.—The patient had lymphogranuloma venereum, tuberculosis and syphilis. She showed no improvement after protracted antisyphilitic therapy. The tissue removed from the ulcer did not show tuberculosis or syphilis. For these reasons we believe that the inflammatory process as studied clinically and pathologically was caused by lymphogranuloma venereum. This case does not meet the diagnostic requirements that were laid down as prerequisites for a diagnosis of osseous disease due to lymphogranuloma venereum. Because of the presence of tuberculosis and syphilis, one cannot say with certainty that the lesion of the sternum was due to lymphogranuloma, but it is highly probable that it was.

SUMMARY

There is much evidence of the constitutional nature of infection with lymphogranuloma venereum, and for this reason it is not surprising that late involvement of the osseous system can occur. Systemic reactions occurring early in the disease, such as anorexia, nausea, vomiting, chills and fever, are mentioned by most authors. Injections of the virus into laboratory animals cause lesions of different systems, depending on the method of inoculation. For example, intraperitoneal injection causes exudative peritonitis; intracerebral injection has produced meningoencephalitis; subcutaneous preputial injection of the virus is followed by involvement of the regional lymph nodes. The virus has been isolated from the mesenteric glands, spleens, livers and lungs of infected animals. It has rarely been demonstrated in the blood. In human beings, extragenital lesions have been reported as occurring on the tongue. Splenic enlargement has been noted. David and Loring [13]

13. David, V. C., and Loring, M.: Extragenital Lesions of Lymphogranuloma Inguinale, J. A. M. A. **106**:1875 (May 30) 1936.

reported a case of lymphogranuloma venereum causing ulcers in the mouth and colon. They stated the opinion that lymphogranuloma venereum should be considered a possible etiologic factor, as in all cases of meningoencephalitis of obscure origin. Von Haam and D'Aunoy [14] successfully isolated the virus from the spinal fluid in cases of lymphogranuloma venereum. They quote Smood [15] and his associates as follows: "In some cases infection with the virus of lymphogranuloma inguinale simulated rheumatic fever, with the pain and inflammatory reactions occurring in large and small joints."

In regard to the mechanism of virus action, Rivers [16] stated:

> If the action of the viruses is not extremely rapid or explosive and if the susceptible cells are capable of multiplication, the primary effect of the active agents is stimulation, leading to cellular hyperplasia. Following the hyperplasia there is usually destruction or necrosis of the cells, which, in turn is attended or followed by a secondary inflammation representing the reaction of the neighboring tissues and the host. The balance between the stimulative and destructive tendencies of the viruses determines whether hyperplasia or necrosis is the predominant part of the pathologic picture. . . . If the action of the viruses is explosive or rapid, as, for instance in Yellow fever and Rift Valley fever, or if the susceptible cells are incapable of division and multiplication, as is the case with nerve cells, then the primary pathologic changes are necrobiosis and lysis of cells.

Lymphatic involvement with perilymphatic reaction is a possible explanation of the destructive lesions of the pubes in cases 1 and 2. The close proximity of the inguinal glands, with their massive infection to the pubes, suggests the possibility that the infection spread by direct extension.

If one considers that most lesions of lymphogranuloma are genital in origin, some adequate explanation must be found for the infection of joints as anatomically distant as the wrist and knees. The mechanism of this spread has not been demonstrated so far.

Our cases have been like the others reported in that there has been no uniformity in the period elapsing between the initial infection and the occurrence of lesions in the bones. Coutts and Banderas Bianchi [17] mentioned the occurrence of arthritis during the second week of the disease. In Reichle and Connor's case the articular symptoms occurred only four months after the onset of the infection. Frauchiger considered that chronic arthritis was present in the cases that he reported. In all of our cases the condition was definitely chronic.

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14. von Haam, E., and D'Aunoy, R.: Is Lymphogranuloma Inguinale a Systemic Disease? Am. J. Trop. Med. **16**:527, 1936.

15. Smood, cited by von Haam and D'Aunoy.[14]

16. Rivers, T. M.: Pathologic and Immunologic Problems in the Virus Field, Am. J. M. Sc. **190**:435, 1935.

17. Coutts, W. E., and Banderas Bianchi, T.: Lymphogranulomatosis Venerea and Its Clinical Syndromes, Urol. & Cutan. Rev. **38**:263, 1934.

The literature reporting osseous and articular lesions associated with lymphogranuloma venereum has been critically examined. In the early phases of the disease arthritic and polyarthritic manifestations may occur, although they are not especially common. Chronic arthritis may occur late in the disease. Except for cases of arthritis, hydrarthrosis and pyoarthrosis, no instances of actual destruction of bone was found. We report 2 apparently proved cases of bone necrosis associated with lymphogranuloma venereum and a third case, in which such an association is highly probable. Comments have been made on the theoretic considerations of bone lesions in this disease. Minimum diagnostic criteria have been presented, which it is hoped will aid further study of the problem of osseous changes associated with lymphogranuloma.

CONCLUSION

Osseous changes in lymphogranuloma venereum are rare, may occur late in the disease and are probably caused by the specific infection. Joints and flat bones are most frequently involved.

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FRONTAL PUNCTURE FOR VENTRICULOGRAPHY

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We are well aware that some neurosurgeons occasionally perform ventriculographic examination through frontal burr holes;[1] however, the numerous advantages of the method have not been sufficiently stressed and it does not at present enjoy the widespread use it deserves. For this reason the following note is submitted.

Since ventriculography was first described[2] the method of choice for ventricular puncture in most clinics has been to make a parieto-occipital opening in the skull[3] and to insert the brain cannula into the ventricular system either in the posterior horn or at the junction of the posterior horn with the body. Difficulties met with in this procedure may be enumerated as follows:

1. The posterior horn in normal persons varies considerably in size. In some cases it may even be absent. Numerous cannula punctures may be necessary before the ventricle is reached.

2. The cannula may enter the glomus of the choroid plexus and produce a hemorrhage into this structure. This produces a misleading or confusing intraventricular filling defect.

3. All too frequently in the interchange of gas for fluid poor filling of the third ventricle results, and the aqueduct and fourth ventricle are not visualized. This is due to the fact that the cannula is in a lateral ventricle at the level of or above the foramen of Monro, and the fluid which is removed is only that from the ventricle tapped plus that from the portion of the opposite ventricle anterior to and above the foramen of Monro (fig. 1 *A*).

4. The need for bilateral ventricular puncture is frequent.

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1. Dandy, W. E.: Cerebral Pneumography, in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1936, vol. 12, chap. 1, p. 89.

2. Dandy, W. E.: Ventriculography Following the Injection of Air Into the Cerebral Ventricles, Ann. Surg. **68**:5, 1918.

3. Horrax, G., in Nelson Loose-Leaf Living Surgery, New York, Thomas Nelson & Sons, 1937, vol. 11, p. 416N. Deery, E. M.: A Method of Ventriculography, Bull. Neurol. Inst. New York **1**:193, 1931.

5. The cannula tract is close to the visual pathways, and blindness [4] (usually temporary) following posterior ventricular puncture is not unknown.

6. In hospitals where ventriculographic examination is not a frequent procedure, adequate operating tables or chairs with proper head rests are not always available.

Frontal ventricular puncture is performed as follows:

The entire head is shaved and prepared. With the patient in the prone position with the head extended, a 3 cm. incision is made just within the hair line above the forehead (10 cm. above the supraorbital ridge) and 2 cm. lateral and parallel to the midline. The skin and subcutaneous tissues are retracted with a mastoid retractor, which also controls the bleeding. A burr hole or trephine opening is made in the bone. The outer layer of the dura is incised with a sharp-pointed

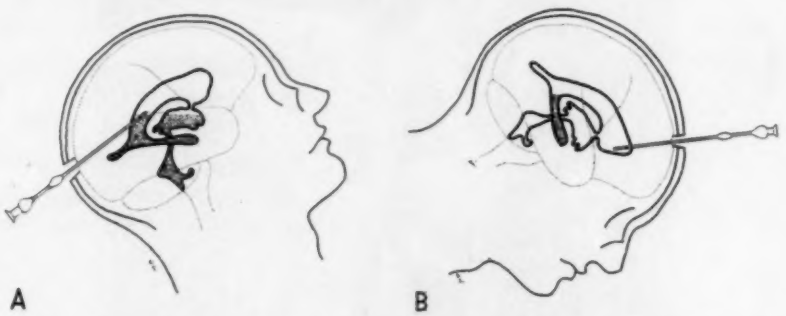

Fig. 1.—*A*, posterior ventricular puncture. The ventricle is tapped at the level of the foramen of Monro. *B*, frontal ventricular puncture. The ventricle is tapped below the foramen of Monro.

scalpel, the edge being grasped and retracted with mosquito forceps. This permits the opening of the inner layer of the dura with greater safety and prevents injury to the underlying cortex. The dura is then opened widely. A small nick is made with the scalpel through the leptomeninges and the pia in the center of a gyrus. The brain cannula is then inserted perpendicular to the surface of the skull and slightly mesially. The lateral ventricle is entered at the junction of the anterior horn with the body. By this method, as compared with the posterior approach, the ventricle is entered with remarkable ease. It is only on rare occasions that more than one needle puncture is necessary. The needle is below the foramen of Monro (fig. 1 *B*) and consequently in this procedure most of the fluid of the entire ventricular system

4. Masson, C. B.: Disturbances in Vision and in Visual Fields After Ventriculography, Bull. Neurol. Inst. New York **3**:190, 1933.

(including the third ventricle, the aqueduct and the fourth ventricle) can be replaced through this single burr hole.

The advantages of this method of frontal ventricular puncture are the following:

1. There is little variation in the anatomy of the ventricular system at the point where the cannula enters it, in contradistinction to the great variation found in the size of the posterior horns. More than one cannula puncture is rarely necessary.

2. The choroid plexus is avoided.

3. Much better visualization of the entire ventricular system is afforded.

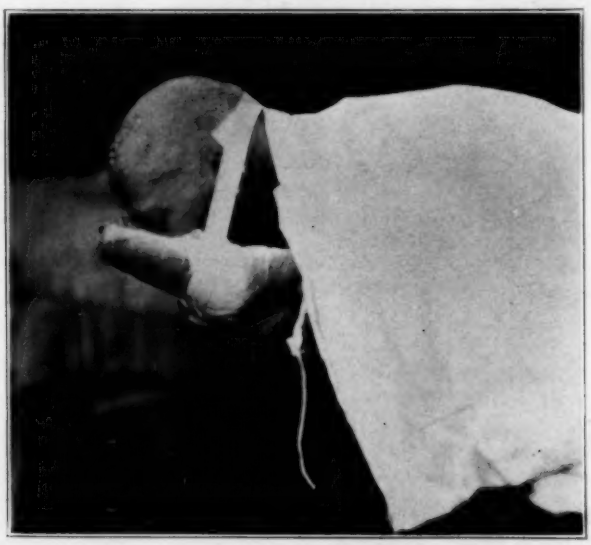

Fig. 2.—Patient in position for frontal ventricular puncture. The cerebellar head rest is in the reverse position.

4. The need for bilateral ventricular puncture is lessened.

5. There is less chance of injuring important cerebral structures.

6. When the patient is in the prone position the intraventricular pressure is higher than when he is in the semirecumbent or sitting position; thus more complete drainage of the ventricular system is obtained.

7. No special operating tables, chairs or head rests are necessary. If a cerebellar head rest is available it is best to reverse it and extend the patient's head (fig. 2). We have frequently used an ordinary operating table, the patient's head being extended by means of a sandbag or a hard pillow placed beneath the chin.

DRAINAGE OF THE COMMON BILE DUCT WITH RESULTANT EXTRARENAL AZOTEMIA

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AND
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This paper is presented to describe a comparatively rare complication following drainage of the common bile duct. On reviewing the literature we found few data on the actual amount of biliary drainage to be expected from a T tube after exploration of the duct. In our experience the average figures for an adult are 300 to 500 cc. per day, with a maximum of 1,500 cc. in an isolated instance. Other investigators have placed a high point at 25 to 30 cc. per kilogram of body weight per day, which for an average person weighing 75 Kg. would amount to 2,250 cc. daily. Walters and his associates [1] in their paper on cholorrhagia following prolonged obstruction reported an output of 2,050 cc. in a single day in 1 patient. In the case here presented there was much more abundant drainage, starting at 1,800 cc. on the first postoperative day.

REPORT OF A CASE

E.K., a 57 year old white man, was admitted to the State of Wisconsin General Hospital on Jan. 27, 1938. The chief complaint was "pain in the stomach." After a fall on Sept. 11, 1937, he had acute paroxysmal abdominal pain, a temperature of 105 F. and jaundice. After a week he was discharged from his local hospital, a bland, fat-free diet being prescribed. At this time the jaundice was clearing. Similar attacks followed with increasing frequency until late in December, when jaundice appeared and persisted. Administration of morphine was necessary for relief of pain in all episodes. Fever was present on each occasion. The color of the stools definitely changed as the jaundice increased or regressed.

The history by systems revealed no pertinent symptoms except a loss of 50 pounds (22.5 Kg.) in the preceding four months. The family history and the social history were essentially noncontributory.

Physical examination showed moderate icterus of the skin and scleras and evidences of recent scratching. The chest was barrel shaped and hyperresonant, with bilateral basal rales posteriorly. The heart tones were distant, and the heart was slightly enlarged to the left, with a soft systolic murmur at the apex, which was transmitted to the axilla. The blood pressure was 120 systolic and 82

From the Department of Surgery, the University of Wisconsin Medical School, and from the State of Wisconsin General Hospital.

1. Walters, W.; Greene, C., and Fredrickson, C.: Composition of Bile Following Relief of Biliary Obstruction, Ann. Surg. **91**:686-693 (May) 1930.

diastolic. Abdominal examination revealed the liver 4 cm. below the right costal margin, with a questionable mass in the area of the gallbladder. Murphy's sign was present. The reflexes were intact. Rectal examination showed prostatic hypertrophy, grade 3.

Laboratory Findings.—The urine was essentially normal except for the presence of bile. The value for hemoglobin was 13 Gm. per hundred cubic centimeters. The red blood cell count was 4,410,000. The white blood cell count was 9,950, with 87 per cent neutrophils, which showed evidences of toxic degeneration. The icteric index was 45. The sugar content of the blood was 93 mg. and the non-

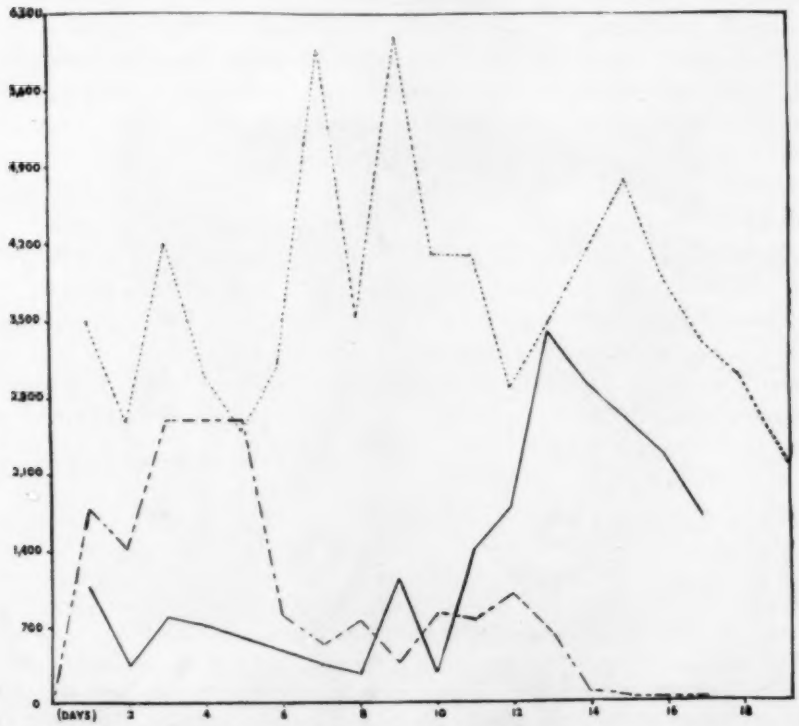

Chart 1.—Graphic representation of output of bile (line composed of one long and two short dashes alternately), intake of fluid (evenly broken line) and output of urine (solid line).

protein nitrogen content 33 mg. per hundred cubic centimeters. The Wassermann reaction of the blood was negative. The value for serum protein was 6 Gm. (albumin 3.9 and globulin 2.1 Gm.). The albumin-globulin ratio was 1.9. The sedimentation rate was 27 mm. in sixty minutes.

Roentgen Studies.—A flat roentgenogram of the abdomen showed no radiopaque bodies. The gastrointestinal series showed an old ulcer in the pyloric canal.

The impression was of obstruction of the common duct due to stone. It was agreed that exploration after surgical preparation was indicated. By February 4 the icteric index was 25; the stools contained bile, and the sedimentation rate was 23 mm. in one hour. On February 10 the abdomen was explored by one of us

(K. E. L.), with the following findings and operative procedure: "There were many adhesions in the right upper quadrant of the abdomen, and the pylorus and duodenum were freed with some difficulty from the mass around the gallbladder. The latter was finally freed, and the gallbladder and cystic duct were found to contain stones. Stones were also palpable in the common duct. The gallbladder was removed retrograde and severed at the junction of the ampulla and the cystic duct. Through this opening five small stones and one large stone were removed. Probes could then be easily passed up into the right and left hepatic ducts and down into the duodenum, and the system was flushed with physiologic solution of sodium chloride. After this a T tube was sutured in place in the common duct and a cigaret drain was placed in the gallbladder bed. The wound was closed in layers in the usual manner."

Postoperatively the patient's course seemed satisfactory except that as early as the first day after the operation it was noted that unusually large amounts of bile

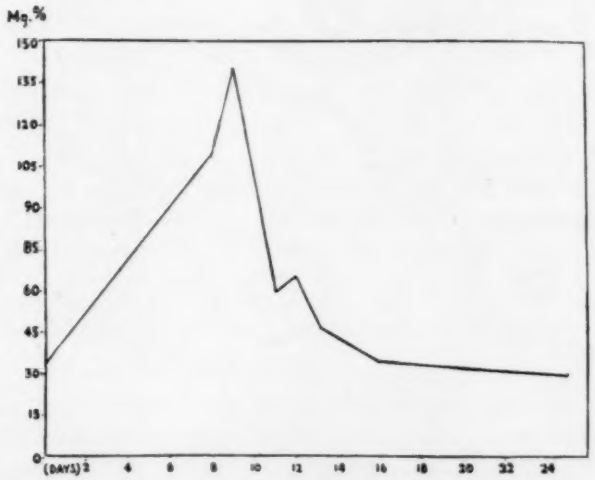

Chart 2.—Nonprotein nitrogen.

were draining through the tube in the common duct. An attempt was made to control this by means of gradual decompression, as suggested by Ravdin and Frazier.[2] This was done by raising the level of the drainage bottle to the height of the patient's bed, thus preventing a siphon-like action. In spite of this procedure, drainage of bile amounting to from 1,800 to 2,600 cc. per day began almost immediately (chart 1). This contrasted markedly with the 300 to 500 cc. observed in most cases, but in view of the patient's apparent well-being we were not unduly alarmed. Liquids were being taken by mouth, but greater amounts of fluid were being lost by biliary drainage. By the sixth day drowsiness, anorexia and fear of impending death ensued, and the patient began to vomit. The carbon dioxide–combining power, determined the following day, was 26.8 volumes per cent (charts 2 and 3).

2. Ravdin, I. S., and Frazier, W. D.: Advantages of Gradual Decompression Following Complete Common Duct Obstruction, Surg., Gynec. & Obst. **65**:11-15 (July) 1937.

The nonprotein nitrogen content had risen to 109 mg. per hundred cubic centimeters, with a creatinine content of 2.7 mg. per hundred cubic centimeters. Therefore the fluid intake was raised to 5,960 cc., given by the oral and parenteral routes, including 160 cc. of a solution of sodium lactate. To complicate the picture further, Wangensteen's negative gastric suction had to be started the next day to control the vomiting. The alkali reserve on the eighth day rose to 39.5 volumes per cent. With the decrease of the alkali reserve it will be further noted that the output of bile decreased to 400 to 800 cc. between the sixth and the ninth day postoperatively. Despite a high fluid intake the patient excreted little urine on the seventh and eighth days, so that dehydration apparently complicated the acidosis.

The chloride content of the blood was not determined until the eighth day after operation, and at that time it was 403 mg. per hundred cubic centimeters. It will be seen (charts 1 and 2) that the nonprotein nitrogen content and the carbon dioxide-combining power rapidly returned to normal as the output of bile continued

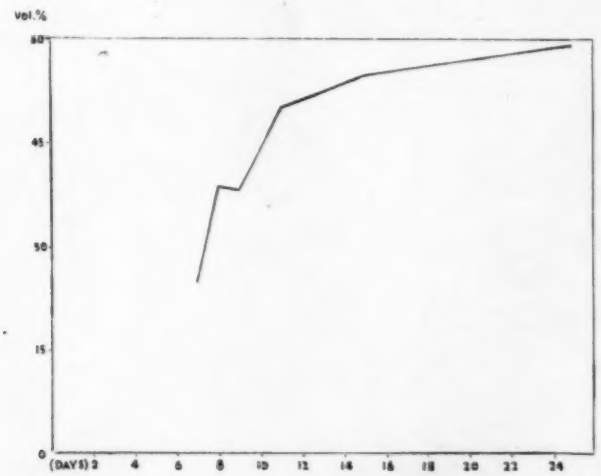

Chart 3.—Carbon dioxide-combining power.

to decrease and the output of urine increased, and the patient returned to a position of positive fluid balance.

COMMENT

It has long been contended that the syndrome of cachexia cholipriva is dependent, at least in part, on the acidosis caused by the loss of sodium salts of the bile acids in the presence of complete biliary fistulas. Okada,[3] McMaster and his associates,[4] Neilson and Meyer[5] and finally Drury

3. Okada, S.: On the Secretion of Bile, J. Physiol. **49**:456-482 (Aug.) 1915.

4. McMaster, P. D.; Broun, G. O., and Rous, P.: Studies on Total Bile, on the Bile Changes Caused by a Pressure Obstacle to Secretion, J. Exper. Med. **37**:685-698 (May) 1923.

5. Neilson, N. M., and Meyer, K. F.: Reaction and Physiology of the Hepatic Duct and Cystic Bile of Various Laboratory Animals, J. Infect. Dis. **28**:510-541 (May-June) 1921.

and his associates [6] with studies on the p_H of bile emphasized the fact that it is a well buffered solution and that considerable amounts of acid are necessary to change its reaction. In this connection Wangensteen showed a patient with total biliary obstruction who was losing only 0.4 Gm. of sodium chloride daily in the bile.

The conclusive experiments of Bissell, Andrews and Brunschwig [7] showed that the carbon dioxide-combining power in cases of complete biliary fistula does not change, at least experimentally. Eight dogs with an average carbon dioxide–combining power of 39.5 volumes per cent and an average value for blood chlorides of 290 mg. per hundred cubic centimeters were used, and a cholecystnephrostomy was done or a permanent biliary fistula produced. After this the animals were studied for periods ranging from twelve to eighty days. The symptoms of acholic cachexia were typical, but the carbon dioxide–combining power averaged 39.5 volumes per cent and the chlorides 293 mg. per hundred cubic centimeters. On the subject of acid-base equilibrium they said in conclusion:

> It seems justified, therefore, to assume that if the typical picture of cachexia cholipriva may be produced without changes in the acid-base equilibrium this factor is not fundamental, and that when reported by others it must be assigned to some intercurrent or indirect cause and must not be considered a fundamental etiologic factor. While acidosis, as reported by many, may be a frequent accompaniment of acholic cachexia and may explain some of its manifestations, it seems wisest to attribute it to infection of the fistulous tract rather than to loss of bile.

Latteri [8] has also reported changes in the carbon dioxide–combining power after experimental studies on the biliary tracts of dogs. This work shows definite decrease in the carbon dioxide–combining power following complete occlusion of the common bile duct. It is not, however, applicable to studies on animals or on subjects with biliary fistulas.

In our case the picture was typical of acidosis, sometimes referred to as extrarenal azotemia, and this was substantiated by a low carbon dioxide–combining power, of 26.8 volumes per cent. However, the factor of infection, with positive cultures of Bacillus coli and unidentified streptococci from the bile on the eighth day, must be taken into account.

An attempt to explain the entire picture of acid-base disturbance necessitates the consideration of several factors. As early as the fifth

6. Drury, D.; Rous, P., and McMaster, P. D.: Observation on Some Causes of Gall Stone Formation, J. Exper. Med. **39**:403-423 (March) 1924.

7. Bissell, A. D., and Andrews, E.: Acholic Cachexia: Experimental Studies, Arch. Surg. **32**:624-668 (April) 1936. Andrews, E., and Bissell, A. D.: Acholic Cachexia: Acid Base Equilibrium, Proc. Soc. Exper. Biol. & Med. **31**:548-550 (Feb.) 1934. Brunschwig, A.; Bissell, A. D., and Andrews, E.: Acholic Cachexia: Pathological Changes, ibid. **32**:41-42 (Oct.) 1934.

8. Latteri, S.: La riserva alcalina nelle stenosi ed occlusioni sperimentali del coledoco, Ann. ital. di chir. **10**:66-83 (Feb. 14) 1931.

postoperative day there was a sense of malaise, and the next day there were frank mental lethargy and drowsiness. The total output of bile during the first six days was 12,800 cc. Urinary excretion steadily decreased to a low point of 310 cc., suggesting approaching anuria. We believe that usually with an alkali deficit the kidneys respond with a greatly accelerated elimination of water and acid and the formation of large amounts of ammonia. In this manner a large amount of the water of the body is excreted. We feel that diuresis and dehydration are part of the phenomena consistently accompanying acidosis in the absence of renal disease. It is true that in this case in contrast to diuresis there was a reduction of the urinary output, but this can be accounted for by the excessive amount of fluid lost through biliary drainage and vomiting.

Peters and Van Slyke [9] disagreed with the statement in Marriott's monograph on anhydremia, that acidosis is one of the phenomena of dehydration. It was difficult for them to see how dehydration can in itself cause an alkali deficit unless the anuria interferes with the renal excretion of ammonia and acid. "In this case one might expect an acidosis similar in nature to that of nephritis. Whether such retention follows dehydration appears not to have been determined."

The negative fluid balance, which was present for several days, amounted at times to 300 to 400 cc. This complication was suggested by Snell and Rowntree, who said that secretion of bile is independent of conditions of fluid intake and electrolyte balance. McMaster, Broun and Rous [4] have shown that after relief of obstruction the output of bile is copious until the elimination of retained biliary constituents has been completed. The bile in this period is much more dilute than normal; but, by the increase in volume, output of bile pigment is elevated during the period of choleresis.

SUMMARY

In our opinion this case emphasizes three facts:

1. The elimination of large amounts of bile through a fistula, at least in the presence of infection, may cause acidosis.

2. Copious drainage of bile may follow drainage of the common duct for obstruction in spite of biliary decompression.

3. Accurate records of total fluid intake and output must be kept in order to eliminate the danger of a negative fluid balance as a factor in the production of acidosis.

9. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, vol. 1.

FATE OF BURIED SKIN GRAFTS IN MAN

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NEWARK, N. J.

Present opinion hypothesizes that epithelium-lined cysts often occur from portions of surface epithelium transplanted into the deeper tissues beneath the skin. This transplantation is believed to follow puncture wounds of the palm and fingers, the point of an instrument or tool having carried a small piece of surface epithelium into the deeper tissues. It is assumed that the small piece of epithelium forms an epithelium-lined cyst which is stimulated to active growth by any form of irritating secondary trauma.

Many investigators have performed experiments on animals by burying strips of epidermis and full thickness skin. In these experiments cysts were observed originating from the epidermis and from the hair follicles. In man, so far as is known, the investigation has been limited to the study of traumatic epithelial cysts presumed to result from injury or operative incision. My observations in microscopic examination of skin buried in human beings differ from the observations of investigators working with animals.

PREVIOUS EXPERIMENTAL WORK

Reverdin [1] expressed the belief that as a result of trauma bits of epidermis are torn off and deposited deep in the corium and that cysts develop from these implanted grafts.

Garre,[2] stated that implantation of epidermis alone produces a smooth-walled cyst, while in the cyst resulting from implantation of a whole thickness skin graft papillae are also present.

Kaufmann [3] produced a cyst beneath the skin of the cock's comb by making a deep oval incision through the skin and suturing the margins of the skin together over the oval section. The buried epidermis gradually took on a rounded form and invariably developed into a cyst. The

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Presented before the Society of Plastic and Reconstructive Surgery at the New York Academy of Medicine, March 24, 1938.

1. Reverdin, J. L.: Des kystes epidermiques des doigts, Rev. méd. de la Suisse Rom. **7**:121, 1887.

2. Garre, C.: Ueber traumatische Epithelcysten der Finger, Beitr. z. klin. Chir. **11**:524, 1894.

3. Kaufmann, E.: Ueber Enkatarrhaphie von Epithel, Virchows Arch. f. path. Anat. **97**:236, 1884.

origin of this cyst from the epidermis was evident, because the cock's comb contains no hair follicles or granular elements to provide another possible source.

Schweninger,[4] in a similar experiment on dogs, produced subcutaneous cysts by burying a piece of skin below the surface. Some of the cysts so produced contained hairs and sebaceous glands in their walls and fat, cholesterol and epidermal scales within their lumens.

Pels-Leusden [5] suggested another possible origin for the epithelial cyst and supported it by experiments on the ears of rabbits. He made an incision through the skin, using a "sharp knife" to prevent the accidental implantation of epidermis during the operation. He then placed an absorbable magnesium disk deep within the corium. A cyst was produced about the foreign body, the lining membrane of which contained all the layers of normal epidermis. Pels-Leusden expressed the belief that such a cyst is formed by proliferation from the epithelium of glands that are unavoidably injured by the incision. He concluded that it is unlikely that in an ordinary injury the tough skin of the palm could be torn off and implanted.

Hesse,[6] in a series of experiments, buried a magnesium disk, catgut and a blood clot beneath the skin and later examined histologic serial sections of the sites of implantation. He demonstrated that epithelization to produce a cyst may take place from the hair follicles and the glandular epithelium without any apparent burial of epidermis. He was unable to find papillae in the walls of any of the cysts produced, however, and he stated that for the development of papillae the implantation of whole thickness skin was necessary.

Davis and Traut [7] produced epithelium-lined tubes and sacs in dogs by transplanting free grafts of whole thickness skin directly onto one of the abdominal muscles. In each animal the fascia was drawn over the graft and the graft was left in place from twenty to forty days. The animal was killed, and the buried skin with the adjacent structures was carefully removed and fixed in solution of formaldehyde. The authors noted the formation of an epithelium-lined tube or cyst resulting from a cylindric growth at the margins of the skin graft. They stated that when the experiments were carried beyond forty days maceration of the epithelial lining of the cavity of the cyst occurred.

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4. Schweninger, E.: Beitrag zur experimentellen Erzeugung von Hautgeschwülsten (Atheromen), Charité-Ann. **11**:642, 1884.

5. Pels-Leusden, F.: Ueber abnorme Epithelisierung und traumatische Epithelcysten, Deutsche med. Wchnschr. **31**:1340, 1905.

6. Hesse, F. A.: Die Entstehung der traumatischen Epithelcysten, Beitr. z. klin. Chir. **80**:494, 1912.

7. Davis, J. S., and Traut, H. F.: The Production of Epithelial Lined Tubes and Sacs, J. A. M. A. **86**:339 (Jan. 30) 1926.

They assumed that this was due to pressure from the contents of the cyst. Histologic observations on the fate of hair follicles and glandular elements in the dermis of the skin graft were not reported.

Zimches,[8] in a series of his own experiments and in experiments performed in association with Wassiljew, buried free strips of full thickness skin in the muscle of dogs. His conclusions, based on studies of implants buried for periods up to two years, were as follows:

1. The epidermis of the implanted skin curves in the shape of a horseshoe, and on about the twenty-fifth day the ends of the horseshoe join, forming a circle or closed cavity lined with epithelium.

2. The cavity of the cyst is partly filled by epithelial debris and broken-down hairs.

3. The cyst continues to grow because the lining epithelium constantly produces cornified epithelium, which is pushed into the lumen.

4. Small cysts may develop from the epithelium of hair follicles.

5. The tendency of surface epithelium when transplanted into other tissue to bend on itself and form a closed cavity represents a definite law and finds its explanation in the general law of epithelial growth.

6. Changing of one kind of epithelium into another or into malignant tissue was not observed.

7. The implanted section of skin heals in its new position and quickly joins the surrounding tissue by means of granulation tissue, which is later organized into connective tissue.

The occurrence of foreign body giant cells in the unlined wall of an epidermal cyst has been explained by Stewart.[9] According to him, the contents of the cyst, whether composed of hair, fat, cholesterol or epithelial debris, have the irritant properties of a foreign body. In those parts of the cyst where the epithelial lining is lacking this irritation produces a type of granulation tissue rich in giant cells.

Wien and Caro [10] stated that the traumatic epithelial cyst is believed to develop as a result of injury to the skin and occurs most frequently on exposed sites, such as the palms and fingers. The probable origin of the cyst is from epidermis torn from the surface and carried into the corium. Such a cyst may also form about a foreign body implanted into

8. Zimches, J. L.: Ueber das Schicksal des in die tieferen Gewebe frei transplantierten Deckepithels in Zusammenhang mit der Lehre von den Epithelcysten, Frankfurt. Ztschr. f. Path. **42**:203, 1931.

9. Stewart, M. J.: On the Occurrence of Irritation Giant Cells in Dermoid and Epidermoid Cysts, J. Path. & Bact. **17**:502, 1912.

10. Wien, M. S., and Caro, M. R.: Traumatic Epithelial Cysts of the Skin, J. A. M. A. **102**:197 (Jan. 20) 1934.

the dermis by proliferation of epithelium from the hair follicles or glandular elements of the skin.

Imakita [11] transplanted particles of skin into the muscle tissue of guinea pigs and noted that hypertrophy and hyperplasia of epidermis and hair follicles were more marked in muscle tissue than in brain. As in his earlier experience with guinea pigs, almost all implants formed cysts at the end of two weeks, and even five months after implantation the epidermis was thicker than in the control section. In a subsequent article [12] the same author came to the same conclusions by counting the mitotic figures.

Okuma [13] buried sections of skin the size of a rice grain in the subcutaneous fasciae of the backs of adult rabbits. The implanted particles of skin invariably caused the formation of a cystlike structure after a more or less definite period. Okuma also noted after transplantation that the sebaceous glands at first atrophy but later tend to resume their function and recover their normal shape.

The experiments reviewed were conducted on animals and dealt with the production of an epidermal cyst by transplantation of epidermis into other tissues and with the production of a cyst from hair follicles when a section of skin of full thickness was implanted or when a foreign body was introduced into the dermis.

In a recent experiment, Paddock and I [14] buried free sections of human abdominal skin from which the epidermis had apparently been removed and excised the grafts for histologic examination at intervals varying from seven days to twelve months. Small portions of the epidermis persisted in spite of attempts at complete removal. This epidermis formed small cystic cavities in the sections up to two months but did not appear in later sections. In the seven and twelve month sections there were small cystic cavities containing horny material but with a complete absence of epithelial lining. Other striking features in the sections were the early complete disappearance of the sebaceous glands and hair follicles, with persistence of sweat glands in all of the buried grafts.

The following work was done as a continuation of these experiments, to confirm the disappearance of the epidermis in buried human skin.

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11. Imakita, T.: Beiträge zur Kenntnis der Implantation der Haut: Ueber die Implantation der Hautstücke in das Muskelgewebe, Acta dermat. **20**:137, 1932.

12. Imakita, T.: Beiträge zur Kenntnis der Implantation des Hautgewebes: Ueber die Bedeutung der Mitosezahl an den Epithelzellen des implantierten Hautgewebes, Acta dermat. **20**:138, 1932.

13. Okuma, M.: Experimentelle Studien über den Entstehungsmechanismus der Epithelzyste: I. Ueber das Verhalten eines subkutan autoimplantierten Hautstückchens, Nagasaki Igakkwai Zassi **14**:94, 1936.

14. Peer, L. A., and Paddock, R.: Histologic Studies on the Fate of Deeply Implanted Dermal Grafts: Observations on Sections of Implants Buried from One Week to One Year, Arch. Surg. **34**:268 (Feb.) 1937.

EXPERIMENTAL PROCEDURE

A free elliptic section of skin and subcutaneous fat was removed from the chests of a number of patients on whom a rib graft operation was to be performed for the repair of saddle nose. The free section of skin and fat was transplanted with the hoarded excess of rib cartilage beneath the skin of the chest (fig. 1). After successful repair of the saddle nose the hoarded rib cartilage was removed from the chest, together with the buried segment of thoracic skin. The cartilage was then removed from the excised tissue and

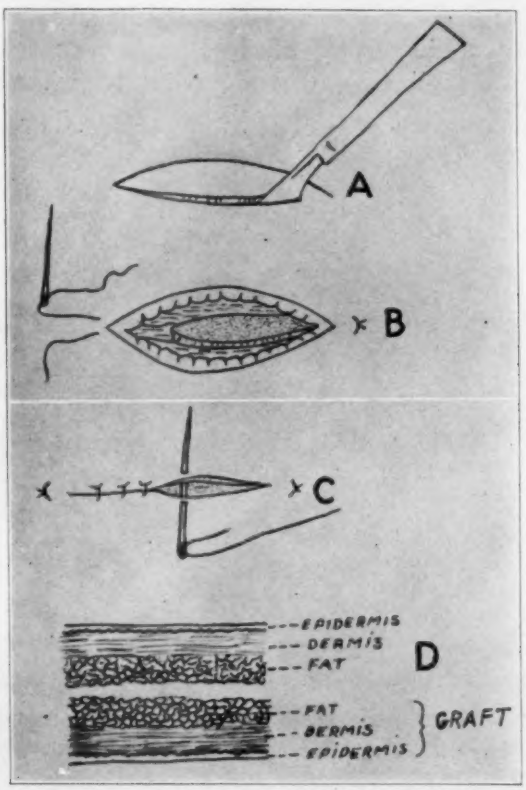

Fig. 1.—Diagrams showing how the skin and fat grafts were transplanted. *A*, elliptic section of skin and fat excised from the chest wall. *B*, section of skin and fat inserted in the wound with the cutaneous surface down and the fat surface outermost. Mattress sutures through the ends of the graft hold it in position. *C*, subcutaneous fat and skin sutured to cover the graft. *D*, cross section of the area of transplantation, showing the relation of the graft to the overlying skin of the chest.

the portion containing the buried skin graft was fixed in Zenker's solution. After sectioning in the usual manner the tissues were stained with hematoxylin and eosin, and after examination they were photographed under high and low power magnification.

DESCRIPTION OF SECTION

Six stages were represented, as follows: two weeks, one month, ten weeks, five and one-half months, sixteen months and twenty-eight months. All of the six transplants were retained by the surrounding host tissue, and the wounds healed by primary intention.

A microscopic study of the two week transplant showed that the graft had fused with the surrounding host tissue except along the surface occupied by the epidermis of the graft. In this location a space was present between the epidermis of the graft and the adjacent host tissue. This space was partially filled with broken-down horny material extruded from the surface of the epithelium and clear fluid material

Fig. 2.—Section of the transplant at two weeks, showing the epidermis of the graft (*A*), the dermis of the graft (*B*), the underlying granulation tissue of the implantation site, containing many giant cells (*C*), and a space (*D*) between the epidermis of the graft and the host tissue.

originating from the host tissue. The host granulation tissue in this location contained many giant cells, large and small round cells and a few polymorphonuclear leukocytes. The epidermal surface of the graft contained indentations and exaggerations of papillae, due probably to contracture of the graft. Sebaceous glands were present in the dermis of the graft but showed definite degenerative changes. Hair follicles and sweat glands were present and were only slightly modified from the normal.

The one month transplant showed the granulation tissue of the host in closer relation with the epidermal surface of the graft. Giant cells

Fig. 3.—Section of the transplant at two weeks, showing a surviving hair follicle (*A*) and sebaceous gland (*B*) in the dermis of the graft.

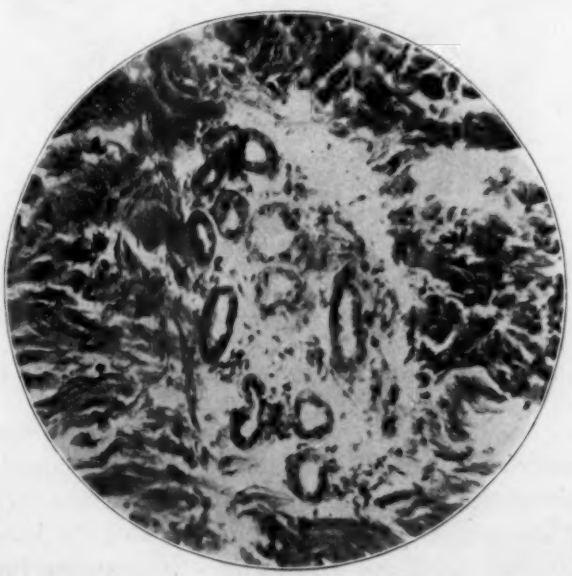

Fig. 4.—Section of the transplant at two weeks, showing surviving sweat glands, somewhat altered in appearance, in the dermis of the graft.

had migrated from the host tissue and appeared to be attacking the epidermal layer of the graft. The epidermis of the graft was thinner than normal in the depths of indentations and in places was separated from the underlying dermis. A higher power magnification showed spaces scattered through the deep layer of the transplanted epidermis which were interpreted as representing degenerative change. The space between the epidermis of the graft and the host tissue was occupied by extruded horny material, fragments of hair from the epidermis and giant cells from the host tissue containing partially digested fragments. The free ends of the epidermis did not appear to be growing in the form of a horseshoe as reported by experimenters with animals, and

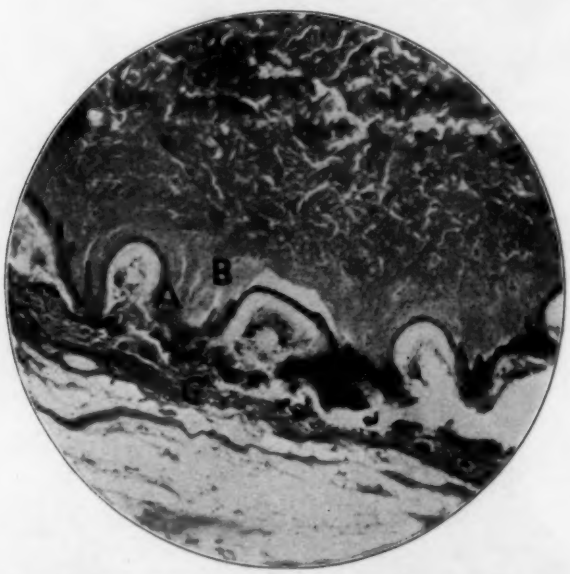

Fig. 5.—Section of the transplant at one month, showing, the epidermis of the graft (*A*), the dermis of the graft (*B*) and the host granulation tissue rich in giant cells (*C*). The epidermis is thin in the depths of the indentations and thicker at the tops of the papillae. The spaces between the papillae are occupied by giant cells and broken-down cornified material and fragments of hair.

the appearance as a whole suggested degeneration and partial absorption of the epidermis. Numerous hair follicles and sweat glands were seen in the dermis of the graft, but no sebaceous glands were seen. On the basis of the absence of sebaceous glands in all of the later sections I concluded that they had entirely degenerated between two and four weeks after transplantation.

A careful study of the sections buried for ten weeks showed no surviving epidermis. The granulation tissue of the host was in close

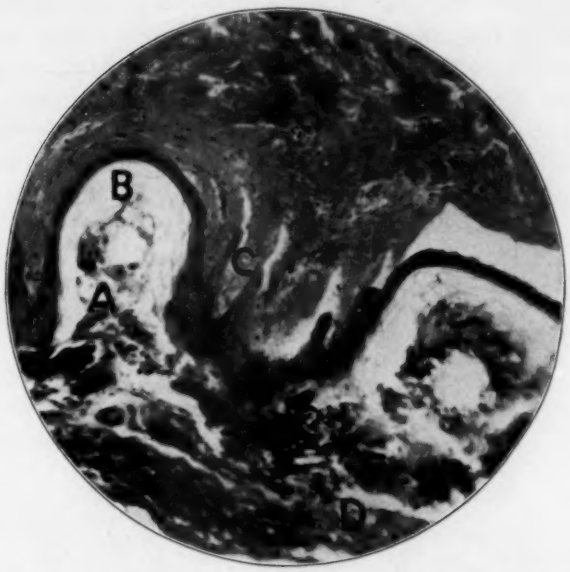

Fig. 6.—Section of the transplant at one month (high power magnification). In the space between the papillae are shown a group of giant cells (*A*) and broken-down cornified material (*B*). At *C*, processes from the epidermis of the graft appear to penetrate into the dermis. *D*, host tissue.

Fig. 7.—Section of the transplant at one month (highest power magnification), showing in detail the host granulation tissue (*A*) in relation to the epidermis of the graft (*B*). Note the group of giant cells (*C*) between the granulation tissue of the host and the epidermis of the graft. Numerous spaces containing clear fluid are present in the epidermis of the graft at *D*.

contact everywhere with the graft. Numerous collections of giant cells were present on the under surface of the graft, where the epidermis had been present at the time of transplantation. Many of these giant cells contained refractile substances which may have represented bits of partially digested epitheluim or fragments of hair. A few hair follicles and numerous sweat glands were seen in the sections. The sweat glands were approximately normal in appearance, but the hair follicles showed degenerative changes and were frequently seen in the midst of a cluster of giant cells. No sebaceous glands were seen in the sections.

The sections buried five and one-half months showed no surviving epidermis or sebaceous glands. Numerous sweat glands were present

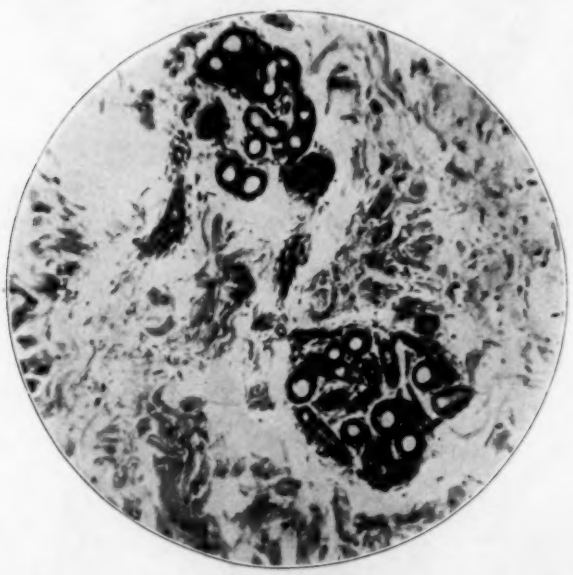

Fig. 8.—Section of the transplant at ten weeks, showing the approximately normal appearance of the sweat gland tubules in the dermis of the graft.

in the dermis of the graft, but only one hair follicle was observed. The graft was intimately fused with the surrounding host tissue, and there was no cellular activity about the surviving sweat glands.

The sections buried sixteen months showed the graft in close apposition with the surrounding host tissue. The region of the graft, indeed, could be located only by the presence of sweat glands in a fibrous tissue stroma located beneath the subcutaneous fat of the overlying thoracic skin. The sections showed no surviving sebaceous glands, hair follicles or epidermis. The surviving sweat glands were approximately normal in appearance and showed no evidence of cyst formation.

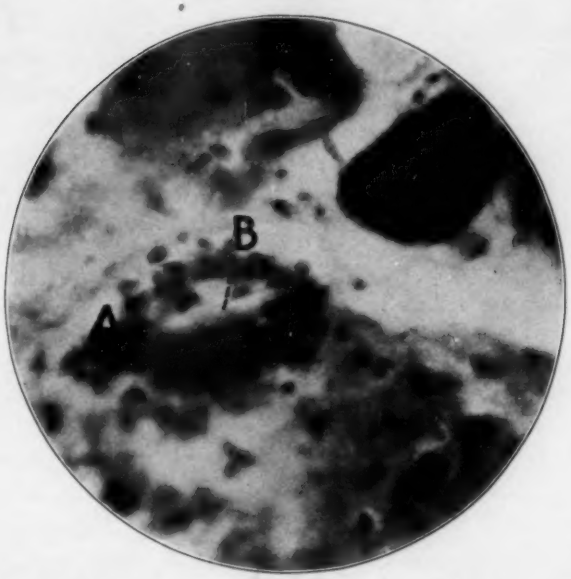

Fig. 9.—Section of the transplant at ten weeks, showing a giant cell (*A*) containing a refractile particle (*B*) believed to be a partially digested remnant of the epidermis of the graft.

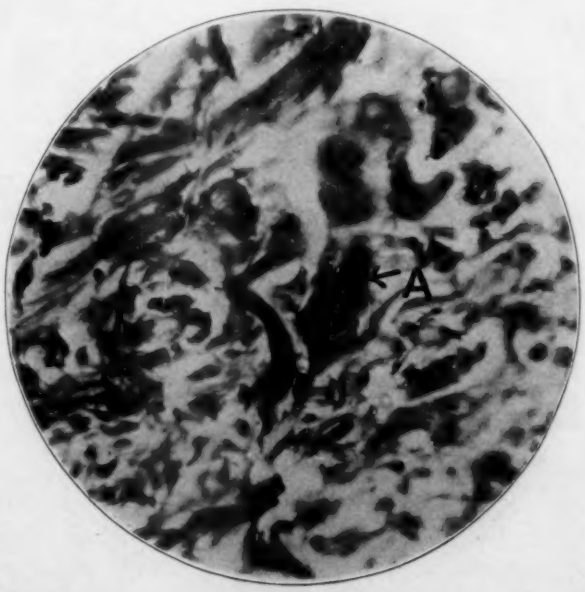

Fig. 10.—Section of the transplant at five and one-half months, showing a surviving hair follicle (*A*) in the dermis of the graft. No remnants of epidermis or sebaceous glands were observed. Sweat glands were present in many of the sections.

Fig. 11.—Section of the transplant at sixteen months, showing surviving tubules of sweat glands in the dermis of the graft. No epidermis, hair follicles or sebaceous glands were observed.

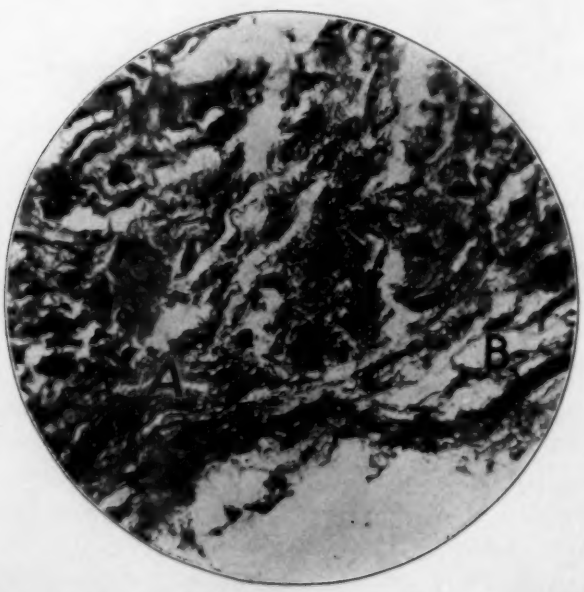

Fig. 12.—Section of the transplant at twenty-eight months, surviving tubules of sweat glands (*A* and *B*). The cells are darkly stained and the lumens extremely small.

The sections buried twenty-eight months showed the graft in close apposition with the surrounding host tissue. There were no surviving epidermis, sebaceous glands or hair follicles in the graft. Sweat glands were present, but they were altered in form, with greatly flattened epithelium. There was entire absence of cellular activity about the surviving sweat glands, and no cyst formation was present. Refractile fragments were present in the buried dermis, which were interpreted as remnants of broken-down hairs.

COMMENT

Comparison of my observations in sections of buried human skin with those of investigators working with buried animal skin shows a rather startling contrast. The epidermis of the human graft shows definite degenerative changes at one month and is entirely absent ten weeks after transplantation. The epidermis of animal grafts turns on itself in the shape of a horseshoe and when the two ends meet forms a closed cyst cavity which progressively increases in size. Zimches studied his grafts in dogs for periods up to two years and found the epidermal lining of the cysts still viable and the cysts themselves increasing in size. Sebaceous glands in buried grafts of human skin have completely disappeared one month after transplantation. Investigators working with animals have reported their survival for much longer periods. Hair follicles in buried human skin were not found after five and one-half months and did not tend to form cysts in the earlier sections. In animals, cysts frequently have been reported as originating from the hair follicles. The sweat glands persisted in all of the buried grafts of human skin but did not lead to cyst formation in any of my sections. The fate of the sweat glands in buried grafts of animal skin was not described, because the skin selected for burial did not contain sweat glands.

One may conclude, therefore, that in the human being buried thoracic skin of full thickness does not lead to cyst formation from the epidermis or from hair follicles, sebaceous glands or sweat glands in the buried section of skin.

In a previous experiment in association with Paddock I [14] buried small bits of abdominal epidermis attached to the dermis beneath the skin of the chests of human beings. Small cysts developed from the buried epidermis and persisted up to two months after transplantation. In later grafts, buried seven months and twelve months, small cystic cavities were found filled with epithelial debris but with complete absence of epithelial lining. It seems apparent that small bits of epidermis produce less reaction in the surrounding host tissue and survive long enough to form small cystic cavities. Eventually, however, the epidermis is completely absorbed.

On the basis of my findings in these experiments with buried human skin, I believe that the implantation theory of cyst formation in the human being is extremely doubtful. One must qualify this statement by assuming that the skin of the palm and fingers acts in the same way after burial as the skin of the chest and abdomen. There is also the possibility that autogenous buried skin in a few persons stimulates less reaction in the host tissue surrounding it and is able to survive and grow into a cyst. The most valuable information obtained from the experiments was the fact that autogenous skin buried in human beings acts differently from autogenous skin buried in animals (guinea pig, dog and rabbit).

SUMMARY

Six grafts of autogenous thoracic skin of full thickness were transplanted, with the subcutaneous fat, beneath the thoracic skin of 6 human beings and removed at intervals varying from two weeks to twenty-eight months.

A microscopic study of sections of these grafts showed that the epidermis survived in the two week graft and in the one month graft but was entirely absent in all of the later grafts.

The sebaceous glands were present in the two week sections but showed definite degenerative changes. No sebaceous glands were observed in any of the later sections.

Hair follicles were observed in all of the sections up to and including those examined at five and one-half months. They were absent in those examined later.

Sweat glands were observed in all of the sections up to and including those examined at twenty-eight months.

Neither cyst formation nor malignant change was observed in any of the sections.

Autogenous full thickness skin buried in the human being acts differently from autogenous full thickness skin buried in animals (dogs).

On the basis of the findings in these and previous experiments with buried human skin, I believe that the implantation theory of cyst formation in man is doubtful.

The sections described in this paper were prepared by Mr. David J. McKinnon, of the Newark Eye and Ear Infirmary. Dr. Royce Paddock aided in interpretation of the microscopic observations.

REVIEW OF UROLOGIC SURGERY

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KIDNEY

Anomaly.—Braasch [1] reviewed the urographic and clinical data in 102 cases of renal fusion observed at the Mayo Clinic from 1930 to 1938. The terms in current use, such as "horseshoe kidney," "lump kidney," "sigmoid kidney" and "crossed renal ectopic," are confusing and should be discarded in favor of a more accurate designation based on the relation of the fused kidneys to the vertebral column. Thus, renal fusion is bilateral when the two renal pelves are situated on opposite sides of the vertebral column, prevertebral when one or both pelves are situated anterior to the midvertebral line and unilateral when both pelves are situated on the same side. Bilateral fusion was observed in 84 cases, unilateral fusion in 13 and prevertebral fusion in 5.

Renal fusion may be inferred in about half the cases from changes in the renal outlines as seen in plain roentgenograms. Stones are a frequent complication (they are observed in 25 per cent of cases of bilateral fusion), and their position aids in the recognition of the anomaly. When the stone is large and partially fills the renal pelvis the cast of the stone will have a deformity similar to that of the shadow observed in a urogram.

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1. Braasch, W. F., and Hammer, H. J.: Renal Fusion: Urographic Data and Their Clinical Significance, Brit. J. Urol. **10**:219-230 (Sept.) 1938.

The following urographic data are of importance in the recognition of bilateral fusion:

1. In 60 per cent of cases one or both renal pelves are below the third lumbar vertebra.

2. In the majority of cases the right pelvis is higher and closer to the vertebral column than is the left pelvis.

3. The calices extend in a direction reversed from the normal, and the most significant diagnostic factor is the characteristic axis of the lower calix, which is directed downward and inward toward the isthmus and may overlap the vertebral column. Occasionally the lower calices of the two pelves are so closely related that surgical separation of the respective renal segments is difficult or impossible. This is true especially in cases of unilateral fusion.

4. The point of insertion of the ureter into the pelvis is frequently lateral or anterolateral instead of mesial.

Although the pelves are situated closer together than is normal, their wide separation does not preclude the possibility of fusion, and although fixation of the renal mass is usual, ptosis of one or both segments can occur and can be demonstrated urographically.

Pyelectasis, caliectasis and ureterectasis occur in 81 per cent of cases of fused kidneys. In some instances the dilatation is not associated with pain or obstruction and is considered a congenital abnormality associated with the anomaly and not a pathologic complication. In other instances the pyelectasis is acquired and is associated with stasis. This point should be checked by delayed retrograde urographic study, for the pain and infection associated with stasis can be relieved in some instances by separation of the two renal segments with nephrolysis and nephropexy.

Torre [2] had occasion to do a heminephrectomy on a man 33 years of age with horseshoe kidney complicated by stone and miliary abscesses. The clinical and pyelographic diagnosis, made preoperatively, was renal lithiasis with ureteral obstruction and acute pyelonephritis on the left in a horseshoe kidney. The two kidneys were united at the lower poles. The operation was followed by uneventful recovery. The horseshoe organ had given no symptoms until the stone developed. Apostematous nephritis in a horseshoe kidney is a condition rarely encountered. The good visual exposure given by the reflector made it possible to recognize easily the line of demarcation between the two kidneys and indicated where the section should be made.

With the means available today to the urologist, the diagnosis of horseshoe kidney has become relatively easy. It remains true, however,

2. Torre, D.: Nefriti apostematosa litiasica sur rene a ferro di cavallo, Arch. ital. di urol. **15**:15-32 (Jan.) 1938.

that "to make the diagnosis, one must think of its possibility," and it is evident that the surgeon does not always think of it. Only with the more extensive use of descending urographic examination will the percentage of preoperative diagnoses increase.

In 169 cases collected by Schilling, lithiasis was present 69 times, hydronephrosis 35 times and tuberculosis 24 times. Tumors have been reported in 13 instances, pyonephrosis in 9 and cysts in 5. A horseshoe kidney may have any of the diseases which attack a normal kidney. Bottez found 16 per cent of such kidneys diseased; Bayer set the percentage at 39, and others have placed it still higher.

Horseshoe kidney demands a proper operative technic in relation to: its modified anatomic position, with ptosis and rotation; its median position; the almost constant presence of anomalous vessels; the existence of an isthmus, and the fixity of the organ. Nephropexy alone does not improve the symptoms that accompany horseshoe kidney, since the low insertion of the vascular pedicle, the anomalous vessels and (frequently) short ureters hinder such reposition. Nephropexy combined with section of the isthmus, however, is a logical procedure. When lithiasis is present, as in the case reported by Torre, pyelotomy must be done in situ, since the organ cannot be exteriorized. Nephrectomy is the operation most frequently done, either because the kidney, owing to its anatomic position, is more subject to destructive lesions or because the surgeon, facing a doubtful outcome, decides promptly on removal rather than on doing an operation in two stages, with the difficulties this would make later. The difficulties of nephrectomy consist in the presence of anomalies of vascularization and in the fact that the isthmus holds the kidneys in a median position that makes exteriorization impossible.

Before section of the isthmus the surgeon must determine whether there are any arteries in the isthmus, must find the exact limits of the two components of the horseshoe mass and must determine whether the ureter of the opposite side runs within the isthmus. It is also important not to leave within the wound a fragment of the removed kidney, in which the excretory passages would be suppressed, and not to suppress by a too comprehensive incision a calix of the opposite kidney. In either instance a fistula would result. One must make sure that ligation of the isthmus does not obstruct the course of the ureter of the opposite side.

Wilmer [3] reported 5 cases of unilateral fused kidney, together with a series of 94 cases collected from the literature. In about 60 per cent of the cases the kidneys were found on the right side. The anomaly appears to be equally distributed between the sexes. In the great majority of cases in which the condition was detected either clinically

3. Wilmer, H. A.: Unilateral Fused Kidney: A Report of Five Cases and a Review of the Literature, J. Urol. **40**:551-571 (Nov.) 1938.

or at necropsy the patients were less than 50 years of age. Unilateral fused kidneys seem predisposed to hydronephrosis and pyelonephritis but not to other renal lesions. This anomaly falls into six classes: (1) elongated kidney, (2) S-shaped kidney, (3) L-shaped kidney, (4) mesial fusion, (5) lump kidney and (6) "superior kidney ectopic." The unilateral fused kidney is seen about once in 7,500 autopsies. Fusion of the kidneys is facilitated by a mechanical obstruction at the bifurcation of the aorta into umbilical arteries. These vessels form a crotch which may force together the ascending blastemas. Great variation exists in position, rotation and vascular supply of the unilateral fused kidney. The most common symptom is pain. The renal mass is usually palpable, especially if it is involved in a lesion. Frequently there are urinary symptoms. The diagnosis can be easily and accurately made by taking a pyelogram, which will show the ureter of the ectopic kidney crossing the midline to terminate normally in the bladder, presenting a "triangle" pyelogram.

Beer and Mencher [4] reported a series of 104 cases of double kidney from the records of the Mount Sinai Hospital. Of the 104 cases, there were 89 of unilateral double kidney (85.5 per cent) and 15 of bilateral double kidney (14.5 per cent).

In 14 cases a heminephrectomy was done, with a single operative mortality. The disease was limited to the upper pole in 4 cases (28 per cent); of the 4 patients, 2 had ectopic ureters. The upper pole and its ureter were removed, the lower half of the kidney being preserved. In 10 cases the lower pole showed involvement, and in these the lower half was removed, the upper portion being allowed to remain. The lesion in 6 cases was pyonephrosis; in 5 cases, hydronephrosis; in 1 case, calculous hydronephrosis, and in 2 cases, multiple calculi. In none of the cases was it necessary to perform a secondary removal of the residual portion.

Stone calculated that in 10 per cent of a series of 30 collected cases secondary nephrectomy was required. It is of interest to note that in 12 of the 42 cases of nephrectomy reviewed by Eisendrath there was no abnormality in one segment; in other words, heminephrectomy would have been the more conservative procedure. In 5 additional cases in his series, technical difficulties prevented a heminephrectomy, and a complete nephrectomy was performed.

In all cases which were followed up by cystoscopic or pyelographic study, good function of the remaining portion of kidney was shown at variable lengths of time after the operation.

It is evident, therefore, from a study of Beer and Mencher's cases that conservatism is most important and that renal tissue should be

4. Beer, E., and Mencher, W. H.: Heminephrectomy in Disease of the Double Kidney: Report of Fourteen Cases, Ann. Surg. **108**:705-729 (Oct.) 1938.

saved whenever possible. This point may be emphasized by reference to a patient who has been living for eleven years with approximately one sixth of the normal amount of renal parenchyma.

Deming [5] stated that the expectancy of life of the unilaterally nephrectomized person depends on (1) the cause for which the kidney was removed; (2) the condition of the remaining kidney, and (3) the social status of the patient. Certain operative procedures applicable to tuberculous and pyogenic conditions are available which diminish the mortality and shorten the postoperative course. The young person whose kidney has been removed for causes other than malignant tumor has a normal expectancy of life. Marriage is permissible for persons who have a normally functioning kidney a reasonable length of time after nephrectomy. Pregnancy is permitted for all healthy women who have not had a malignant lesion.

Tumor.—Kerr [6] reported 14 cases of renal neoplasm in children treated by irradiation with roentgen rays followed by operation. Two patients are still alive and without evidence of disease fifty-nine and fifty-two months respectively after admission to the hospital. One had previously been shown to have pulmonary metastasis. Operation should not be deferred beyond the time of continued regression of the tumor. It is worth while to irradiate metastatic lesions and local recurrent lesions intensively.

Hyman and Wilhelm [7] discussed the differential diagnosis of renal and suprarenal tumors. They stated that tumors of the upper pole of the kidney and in the suprarenal region may, for practical purposes, be considered under the following headings:

1. Cyst
2. Inflammatory exudate or abscess
3. Neoplasm of the upper pole of the kidney
4. Neoplasm in the suprarenal region
   (*a*) arising from the adrenal gland
   (*b*) not arising from the adrenal gland
5. Splenic enlargement

Tumors arising in the suprarenal region, when they attain a large size, dislocate the kidney but do not usually distort or obliterate the upper calices. Intrinsic renal tumors, on the other hand, often encroach

5. Deming, C. L.: The Future of the Unilaterally Nephrectomized Patient, Tr. Southeast. Br., Am. Urol. A., Nov. 5, 1937, pp. 2-10.

6. Kerr, H. D.: Treatment of Malignant Tumors of the Kidney in Children, J. A. M. A. **112**:408-411 (Feb. 4) 1939.

7. Hyman, A., and Wilhelm, S. F.: The Differential Diagnosis of Renal and Suprarenal Tumors, J. Urol. **40**:737-751 (Dec.) 1938.

on the outline of the renal pelvis and calices. Blood in the urine also points to intrinsic renal tumor.

Intravenous and retrograde pyelographic procedures are of great value in demonstrating renal and suprarenal tumors. Minimal pyelographic changes, such as the flattening or absence of a minor calix, may be the sole sign of a large tumor. Displacement of the kidney, especially on the left side, is significant.

Perirenal insufflation is of limited value. A case of collapse following its use was reported. The authors stated that this method should be employed with great caution.

The degree of renal mobility is determined by taking roentgenograms with the patient in the Trendelenburg and in the "reverse Trendelenburg" position. Fixation of the kidney has been found in cases of perinephritis and of infiltrating carcinoma.

Lucké [8] stated that the leopard frog is commonly affected with adenocarcinoma of the kidney. As in the case of mammalian neoplasms, this tumor remains localized when small and in its early stages, but when large it frequently forms secondary tumors in distant organs. Dissemination usually takes place by way of the blood stream. Lucké reported 22 new examples of metastasis. His observations of frequent metastasis make the evidence for the malignancy of this tumor complete.

Infections.—Ball [9] stated that infections of the kidney by staphylococci are relatively rarely seen. They usually involve the cortex, are hematogenous and are commonly secondary to suppurations in the skin.

Three types of lesions are recognized. Lesions of the first type, multiple minute abscesses studded throughout the renal cortex, are seen in cases of severe acute pyemia associated with such diseases as acute osteomyelitis type. The second type, a superficial triangular septic infarct just under the renal capsule, is probably present and seldom seen in patients in whom a perinephric abscess heals after adequate drainage has been instituted. The third type is the lesion commonly found deep in the cortex and known as "renal carbuncle," which results in formation of a persistent fistula after drainage of the perinephric abscess and which will not heal until the kidney is removed, or if it heals will be followed by a recurrence of symptoms.

In all attempts to reproduce these lesions experimentally, intravenous injections of cultures of Staphylococcus aureus in varying doses were made in rabbits. The animals were killed at the end of varying periods up to two weeks. It was learned that lesions similar to those found in man can be produced in the rabbit; that the abscesses formed

8. Lucké, B.: Carcinoma of the Kidney in the Leopard Frog: The Occurrence and Significance of Metastasis, Am. J. Cancer **34**:15-30 (Sept.) 1938.

9. Ball, G.: Staphylococcal Infections of the Kidney, Brit. J. Urol. **10**:323-336 (Dec.) 1938.

by the introduction of staphylococci into the blood stream are more likely to form in the kidney than in other organs; that they are slow in their formation; that both superficial and deep lesions are formed, the latter, resembling the "renal carbuncle" of man, being slowest in their formation, and that the resistance of the animal determines the number and rapidity of development of the lesions. It was disappointing that a perinephric abscess did not form in any of the animals, as it was hoped to demonstrate its relation to a superficial renal infarct.

The disease occurs more often in men than in women. There may be a period of two to eight weeks, sometimes much longer, after the cutaneous lesion occurs before there is evidence of general infection. General infection is characterized by malaise, fever, rapid pulse and leukocytosis without localizing symptoms either in the kidneys or in other organs. These symptoms may become chronic and may continue for a long period before there is any clue to their origin. The length of this period depends on the depth of the lesion from the surface of the kidney. The urine may be normal even in advanced stages except for a few leukocytes, erythrocytes, a trace of albumin or a few staphylococci observed after centrifugation.

Ball reported 5 cases of renal carbuncle and concluded that in arriving at a diagnosis these points should be kept in mind: 1. There is a history of a primary staphylococcic lesion, which may be present at the time of formation of the renal focus or may have healed months before. 2. In the early stages, absence of symptoms relating to the urinary tract is a common feature. 3. There is invariably a high leukocyte count. 4. When the condition is suspected, pyelographic procedures may be a most useful method of investigation in arriving at an early diagnosis of the renal lesion. If intravenous pyelographic procedures are used, it is possible that the dye may fail to show in the affected kidney; should this occur or should the diagnosis still be doubtful, there should be no hesitancy in resorting to the retrograde method. Widening or obliteration of the calices is the picture commonly obtained. With the superficial renal lesion it is possible that no defect may be found, but if the lesion is large or is of the deep variety this method of diagnosis is invaluable. 5. At a later stage, when there are obvious physical signs in relation to the kidney, as a rule a perinephric abscess has already formed. It is worth while to obtain a pyelogram even at this stage as an indicator for subsequent treatment. 6. If there is still doubt, the loin should be explored surgically.

Treatment should be as conservative as possible. Drainage of a perinephritic abscess may suffice. The change in the pyelograms and the clinical progress will determine whether a subsequent early nephrectomy is indicated.

If a perinephritic abscess is not found, pyelographic examination will determine whether early removal is indicated and whether a prolonged illness can thereby be prevented.

Ryle [10] divided staphylococcic perinephritis into two types, the septicemic and the nonsepticemic. In the former the toxic symptoms overshadow the local signs of perinephritis. In the latter a renal abscess is the only metastatic focus to be discovered; the onset is insidious, and the symptoms are not severe.

Ryle said that staphylococcic perinephritis complicating a renal carbuncle is a disease of early or middle adult life and is rare in childhood. All of his patients were males, and their ages varied from 9 to 45 years.

In 9 of the 11 cases the etiologic factor was a cutaneous boil or carbuncle. The interval between the primary infection and the occurrence of a renal metastatic lesion varies from two weeks to two months, although the staphylococcus may be dormant for years.

With staphylococcic septicemia the prognosis is poor. Of Ryle's 13 patients, 7 (54 per cent) died; 3 of the 13 patients had renal foci with perinephritis, and only 1 of these 3 recovered.

In the nonsepticemic group the 8 patients who had perinephritis all recovered, 6 of them after simple drainage and 2 without surgical intervention.

Treatment generally should be conservative.

Dukes [11] said that the finding of staphylococci in the urine when contamination and faulty collection have been ruled out is an important observation because infection of the various parts of the genitourinary tract with these organisms has distinct clinical significance.

The characteristic lesion in the kidney is cortical suppuration or carbuncle. The infection is embolic from abscesses elsewhere or from the upper portion of the respiratory tract, and the suppuration may spread to the perinephric space or pus may discharge into the pelvis.

In the early stages the urine does not contain pus, but the centrifuged specimen may show a few clumps of gram-positive cocci and cultures may show a growth of Staph. aureus. Secondary infection with Bacillus coli occurs in about half the cases and tends to persist longer than the primary infection.

Surgical treatment is necessary in many cases, but mild infections may disappear spontaneously or may respond to medical treatment.

Staphylococcic infection of the bladder is uncommon except after instrumentation or in the presence of obstructions, diverticula, malignant

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10. Ryle, J. A.: Perinephritis, Brit. J. Urol. **10**:337-347 (Dec.) 1938.

11. Dukes, C. E.: The Clinical Pathology of Staphylococcal Infections of the Urinary Tract, Brit. J. Urol. **10**:373-378 (Dec.) 1938.

growths or calculi. It may be the cause of cystitis with alkaline incrustation and a factor in the formation of stone.

Staphylococcic urethritis and prostatitis frequently follow gonorrheal infections, or they may be primary infections and may be transmitted by sexual intercourse. Extension to the epididymis is not uncommon, with formation of an abscess which involves the testicle.

Some strains of staphylococci are capable of splitting urea, with the formation of alkaline urine. When obstruction and stasis are present with these infections, stones composed of the earthy phosphates are likely to be formed with staphylococci as nuclei. The term staphylococci can be applied to many of these urea-splitting gram-positive diplococci only in a general way.

The mixed character of these urinary cocci is shown by the work of Stadnichenko,[12] who studied thirty strains of gram-positive cocci isolated in cases of genitourinary infection and found fourteen strains which decomposed urea. Eight of these produced an orange-colored growth on agar, and six showed a white growth. No cultural characteristics other than fermentation of dextrose and sucrose were common to these fourteen strains.

Dukes said that the question whether staphylococci in the urine are of pathologic significance can be decided generally by the patient's clinical condition, the manner of collection of the specimen and other findings in the urine. Staph. aureus is usually pathogenic with albus strains. The following points may help to determine whether the organism is contaminated or of clinical significance, although only in exceptional cases is it worth while to make such a determination.

1. Hemolytic staphylococci are more likely to be pathogenic than nonhemolytic strains, although this cannot be accepted as an invariable rule.

2. Staphylococci which rapidly liquefy gelatin are more likely to be pathogenic than nonliquefying strains.

3. Some strains of staphylococci secrete a ferment known as coagulase. The presence of this ferment can be shown by adding a small quantity of a culture to oxalated rabbit plasma and incubating the mixture at 37 C. for three hours. The occurrence of coagulation is to be taken as evidence of pathogenicity in the strain tested.

4. Toxic substances may be shown to be present in filtrates of broth cultures of some strains of staphylococci. When injected into the peritoneal cavities of laboratory animals these toxic substances excite peritonitis, and under the skin they give rise to cellular infiltration and to formation of an abscess. Virulent staphylococci are likely to produce more of this substance than nonvirulent ones.

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12. Stadnichenko, A. M. S.: Thirty Strains of Gram-Positive Cocci Isolated from Cases of Genito-Urinary Infections, J. Bact. **17**:303 (May) 1929.

Renal Tuberculosis.—A study was made by Emmett and Kibler [13] of 1,131 consecutive patients on whom nephrectomy was performed for renal tuberculosis at the Mayo Clinic between 1912 and 1932. The purpose of the study was to determine, if possible, the prognosis after nephrectomy on the basis of observations obtained in clinical investigation of the so-called good kidney prior to operation. From this study it was hoped to be able to bring about a closer agreement among urologists as to the amount of clinical investigation necessary to determine the character of a "good" kidney before removal of the "bad" kidney is advised. The study showed the results from five to twenty years after nephrectomy. The patients were grouped according to the type of investigation carried out on the "good" kidney and also according to the findings obtained from such studies.

Seven tables indicated in detail the interesting results, which may be briefly summarized as follows: In order to make a fairly accurate prognosis, catheterization of the good kidney to determine the amount of pus being secreted is imperative. The presence of normal urine leads to a favorable prognosis, and statistical data indicate that the patient may expect approximately a 43.5 per cent chance of a five year cure, a 65.2 per cent chance of being cured or improved in that period and only a 20.3 per cent chance of death within five years. If, in addition to this, inoculation of a guinea pig gives a negative result and a positive acid-fast stain is not obtained, the patient's chance of dying within five years will drop to 13.3 per cent, his chance of a five year cure will be increased to 50.3 per cent and his chance of being either cured or improved will increase to 75.2 per cent. On the other hand, if the results of inoculation of the guinea pig are positive, the patient's chance of dying within five years increases to 41.8 per cent and his chance of a five year cure drops to 21.8 per cent. These figures are dramatic and demonstrate that the results differ greatly in cases in which the urine from the good kidney is normal, depending on whether the results of inoculation of the guinea pig are positive or negative.

The question then arises: Should a positive result from a guinea pig test corresponding to the good kidney, in spite of absence of pus in the urine, be considered a contraindication to surgical operation? It must not be forgotten that 21.8 per cent of the patients were cured, that a total of 36.4 per cent were either cured or improved at the end of five years and that 30 per cent were either cured or improved at the end of ten years. Certainly almost any one who had the disease would be willing to submit to operation if given a 30 to 36.4 per cent chance of improvement for from five to ten years. If other factors do not consti-

13. Emmett, J. L., and Kibler, J. M.: Renal Tuberculosis: Prognosis Following Nephrectomy, Based on Preoperative Observations in the "Good" Kidney, J. A. M. A. **111**:2351-2356 (Dec. 24) 1938.

tute contraindications to surgical operation and if the excretory urogram of the good kidney is within normal limits, it seems that a positive result from a guinea pig test should by no means be considered a contraindication to surgical measures, although it would considerably alter the prognosis. The common procedure, therefore, of performing nephrectomy in such cases without awaiting the report of the results of inoculation of animals would appear to be justified.

When pus is found in the catheterized specimen of urine from the good kidney, the problem is radically altered. Because of the small number of such cases in this series it is difficult to make as far-reaching statements as have been made concerning cases in which the urine was microscopically normal. However, the study suggests that if more than 3 pus cells per high power microscopic field are found and if the guinea pig test or the stain gives a positive result, the prognosis is poor, and it is questionable whether operation is warranted. In such cases, no doubt, fairly advanced bilateral renal tuberculosis is present and the possibility of clinical improvement of the better of the two kidneys after operation certainly is questionable. If there is a small amount of pus, if inoculation tests and stains give negative results and if the excretory urogram is normal, the prognosis seems to be reasonably good and possibly surgical measures are worth a trial. This is true especially if there are not more than 10 or 15 pus cells per high power microscopic field in the centrifuged specimen of ureteral urine.

Perinephritic Abscess.—Astraldi, Fernandez and Brea[14] reported a case of purulent perinephritic fistula which had been draining for five months when it came under their observation. The history given by the patient was as follows: Six or more months previously he had had an interdigital infection of the right hand, which had to be opened surgically after symptoms had been present for two weeks. A week or so later he became feverish again and began to have persistent pain in the right lumbocostal region. Three weeks later his urine became purulent. For this he was subjected to a lumbotomy, and an abscess was drained of a large amount of pus. A persistent discharging fistula remained, which at length brought him to the authors' observation.

The first clinical impression was of a perirenal purulent fistula that might be due to a small abscess or to a foreign body (possibly an overlooked instrument), although the roentgenogram did not reveal any such objects. A sound was inserted in the fistulous tract, and dissection was carried along its course, which ran obliquely downward, inward and backward. After resection of 6 to 8 cm. of the fistula, it was found

14. Astraldi, A.; Fernandez, J. S., and Brea, L. M.: Fistula purulenta lumbar: Osteitis vertebral no tuberculosa, Rev. argent. de urol. **7**:298-304 (Sept.-Oct.) 1938.

to be oriented toward the vertebral column and not toward the perirenal capsule. A second study of the roentgenogram revealed osteitis of the third lumbar vertebra. The fistula was resected at this level and was drained, and a suture was placed. Examination of the pus had revealed a pure culture of staphylococci. The fact that the lumbar or perirenal lesion had appeared during defervescence from a suppurative interdigital process seemed to point to a direct relation between the two conditions.

The rapidity with which the abscess had formed, one week after the infection of the finger and its roentgenologic character, showing osteitis of the pure vertebral type, which affects the disks, supported the diagnosis of staphylococcic osteitis and excluded almost definitely the possibility of a tuberculous lesion with a preexistent ossifluent abscess flaring up as the result of a common interdigital infection.

The question arises: Was it this osteitis that secondarily brought about the formation of a perinephritic or pararenal abscess, which was primarily operated on? It seems difficult to doubt it. The vertebral osteitis and osteomyelitis, in an attempt to find drainage, gave rise to the perinephritic (or better, pararenal) abscess. To this the authors answer yes, because the dissection of the fistulous tract led directly to the vertebral region, without any view of the perirenal region during its course; and it was this fistulous tract that was drained in the first operation.

The condition in this case falls definitely into the category described by Tavernier in his discussion of the frequency of "false Pott's disease." According to him, the onset of these abscesses is sudden and febrile; the pain that accompanies them comes on with extreme rapidity; puncture affords no relief, but incision does; the fistula drains promptly unless a bony sequestrum maintains it, in which case the suppuration is more prolonged and refractory than in even the worst examples of true Pott's disease. The first three of Tavernier's requirements were fulfilled absolutely. As for the chronicity, which, according to Tavernier, would be interpreted as due to a sequestrum, the authors were unable to say whether one existed or not, since it was not looked for.

Hydronephrosis.—Egger [15] injected the arteries of hydronephrotic kidneys. Most of the specimens were from men with prostatic enlargement and obstruction, and Egger took roentgenograms of the visualized arterial system. The changes he observed explain how changes in the circulation affect the function of the hydronephrotic kidney. Back pressure destroyed the renal function, causing obliteration of the arteriae interlobares by pressure and by dilatation of the calices, and thus created

15. Egger, K.: Die Veränderungen des Nierenarteriensystems in der Hydronephrose und ihre Beziehungen zur Nierenfunktion, Ztschr. f. urol. Chir. u. Gynäk. **44**:138-152 (July) 1938.

ischemia of the renal parenchyma. The same mechanism causes an obstruction of the interlobar veins and venous stasis. This ischemia and venous stasis in connection with the increased pressure in the renal pelvis cause atrophy of the renal parenchyma. If the increased pressure of the renal pelvis is gradually reduced—for example, by emptying an overdistended bladder—the atrophied renal parenchyma may recover by an increased flow of blood. Sudden emptying, on the contrary, causes a large volume of blood to flow into the diseased arterial system under high pressure, reduces stasis and at times causes an even further reduction of renal function, sometimes resulting in death.

Cysts.—Wehrbein [16] reported a case of extravasation of urine due to rupture of a renal cyst with later encapsulation He stated that in most cases perirenal extravasation is due to traumatic rupture of the kidney.

The case reported by him presented a different problem in diagnosis, because the extravasation was atraumatic. The patient was a man aged 62 who had a sudden sharp pain in the region of the left kidney. He refused cystoscopic examination, and a definite diagnosis was not made at the time of his first entry to the hospital. On his second entry there was still pain in the left renal region, he had lost weight and a soft mass was felt in the region of the left kidney. Cystoscopic examination revealed a continuous drip of urine from the left kidney, such as occurs in cases of hydronephrosis. The kidney was explored, and a large cyst, apparently containing urine, was found. The kidney was pushed upward and the lower pole outward. The cyst and kidney were removed. Examination of the specimen showed a moderately hydronephrotic kidney with two intramural cysts which extended from the dilated middle calix to the capsule. In the capsule a small hole was seen, through which urine had become extravasated into the perirenal fat. The wall of the extrarenal cyst was made up of fibrous tissue of inflammatory origin and did not show any epithelial lining. The fluid in the cyst contained 16 mg. of urea per hundred cubic centimeters and was sterile.

Wehrbein assumed that the very thin wall of the cyst ruptured owing to some hydronephrotic distention and that urine became extravasated into the perirenal space, causing pain, fever and peritoneal irritation with ileus. An inflammatory reaction resulted in walling off of the urine, and with this the irritation of the peritoneum ceased and the ileus disappeared.

De Surra Canard, Amestoy and Bonfiglio,[17] on the basis of a case observed, discussed the anatomopathologic characters of pararenal serous cysts, of which the most striking are those pointed out by Lecene and

16. Wehrbein, H. L.: Urinary Extravasation Due to Rupture of a Renal Cyst with Subsequent Encapsulation, Brooklyn Hosp. J. **1**:33-36 (Jan.) 1939.

17. de Surra Canard, R.; Amestoy, J. M., and Bonfiglio, O.: Quiste seroso pararrenal, Rev. argent. de urol. **7**:317-324 (Sept.-Oct.) 1938.

Leriche. Such cysts are unilateral and of variable size and are included within the fatty capsule of the kidney; they are round, with a smooth surface and of a color related to the contents. The most common site of implantation is on the anterior aspect of the kidney. They become attached to the vascular pedicle and acquire a contact relation with the excretory passage. They develop downward, inward and forward; they form no adhesions to the peritoneum and are crossed by the colon.

The evolution of these cysts is silent, and their discovery is always accidental. The first symptoms are likely to be in the digestive system, on the same side as the cyst. Frequently constipation is the first sign. Usually there are few or no urinary symptoms; in some cases pollakiuria or hematuria appears early. Palpation of the abdomen reveals a tumor with retroperitoneal characteristics, recognized as renal by its movement, which is synchronous with that of the kidney when there are no adhesions. One special peculiarity is the transverse movement that occurs on changes in the position of the patient; the cyst is felt under the examining hand and is due to the anterior implantation. Histologically it consists of endothelial cells, cuboid or flat, implanted on a fibrous capsule in which are elastic fibers and smooth muscle fibers.

Most writers agree that treatment should always be surgical, since, despite its benignity, the cyst is a progressive growth. Opinions differ, however, as to technic and the best mode of approach. While de Surra Canard, Amestoy and Bonfiglio preferred the extraperitoneal route, their desire in this case to explore the abdominal cavity led them to make a transperitoneal approach with a transverse incision. Separating the ascending colon and the great omentum, they saw the tumor protruding behind the posterior leaf of the peritoneum, which they incised with care. Recognizing its cystic nature, they punctured it, since its removal whole would have required too great a breach in the peritoneum, its size being that of a fetal head at term. It was possible to free it on the anterior surface, but its close association with the region of the hilus in its implantation, with large vessels in intimate relation to the wall of the cyst, made its removal difficult; an attempt to section these vessels between ligatures revealed that their walls were too friable and that they tore in the grasp of the forceps. It was then decided to resect all of the cyst except this vascularized portion, which was left behind; at this level hemostasis was made by sutures, and the portion of cystic endothelium remaining in situ was touched with phenol to prevent recidivation. The postoperative course was uneventful, and the wound healed by first intention.

Only 5 other cases have been found in the literature in which the growth corresponded with the accepted description of a pararenal serous cyst. All the patients were women between the ages of 15 and 62 years.

Pyelonephritis.—In reviewing 9,888 autopsies performed in the years 1931 to 1937 at Fahrs' pathologic institute in Hamburg, Hage [18] found 598 cases of ascending nephritis and 69 cases of pyelonephritic contracted kidney. The incidence of contracted kidney was greater among women than among men, but that of pyelonephritis was about equal in the two sexes, as well as the incidence on the right and the left side. In men, pyelonephritis and pyelonephritic contracted kidney are more common in the later decades of life; in women they occur much earlier. In men the primary disease usually can be found, but not in women. Hypertrophy of the prostate gland is responsible for the frequency of pyelonephritis in old men; pregnancy accounts in a large number of cases for the occurrence of the condition in women. The mode of infection could be found in only a small number of cases. In cases in which the source of infection could be traced, it usually ascended from the lower portion of the urinary tract. Hage stated that pyelonephritic contracted kidney is a very serious disease compared with atrophic glomerulonephritis and nephrosclerosis and that it is much more frequent than either. This is of great importance in the clinical evaluation of urinary infection.

Aneurysm.—Kastner [19] reported a case of aneurysm of the renal artery, of which he was able to find only 6 recorded cases in which the condition was diagnosed and treated. He reported the case of a woman 80 years of age who had hematuria of six months' duration. She had recently had a severe hemorrhage, which overdistended the bladder. The right kidney was found to be the source of the bleeding, and nephrectomy was done. The kidney contained an old aneurysm (the size of an apple) of a branch of the renal artery, which was sclerotic. There was also a recent perforation of this aneurysm into the renal pelvis.

Renal Function.—Gaudin and Cabot [20] stated that it has not been proved that damage to a kidney subsequent to obstruction is progressive and leads finally to death of the kidney. They concluded that the persistence of obstruction and the supervention of infection are of definite but unevaluated importance. They emphasized the fallacy of tests of renal function in the presence of obstructive lesions and again drew attention to the remarkable recovery of apparently functionless kidneys after surgical drainage. Three recent cases were presented which illustrated these points.

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18. Hage, W.: Pathologisch-anatomische Statistik der Pyelonephritis und pyelonephritischen Schrumpfniere, Ztschr. f. urol. Chir. u. Gynäk. **44**:172-181 (July) 1938.

19. Kastner, J.: Nierenaneurysma, Ztschr. f. Urol. **32**:442-444 (July) 1938.

20. Gaudin, H. J., and Cabot, H.: The Reestablishment of Function in the Chronically Nonfunctioning Kidney Following Removal of Obstruction, Proc. Staff Meet., Mayo Clin. **13**:388-391 (June 22) 1938.

In these cases, although there was presumptive evidence of a kidney in which nonfunction had persisted for from six to ten years, prompt return of function followed surgical removal of the obstruction in each case. The authors pointed out that a functionless kidney does not of itself give rise to pain and that pain, when present, is evidence that the organ is capable of function. Decision concerning the advisability of nephrectomy must be made at the time of operation. In the case of stone in the middle or lower third of the ureter, it may be justifiable simply to remove the calculus without exploring the kidney, especially when there is a history of recent pain.

The authors stated the opinion that such conservative management will preserve many valuable kidneys which otherwise might be unnecessarily sacrificed.

Papillary Necrosis.—Alken [21] gave a description of what he considered a new pathologic entity, renal papillary necrosis. This condition usually occurs in diabetic persons with pyelonephritis. In some cases the kidneys show characteristic changes. Inflammatory processes localize at the base of the papilla, where a narrow zone of destruction occurs. The papilla then becomes necrotic, drops into the renal pelvis and may be passed through the ureter, causing hematuria and renal colic. The diagnosis is based on the fact that the patient has diabetes; there are urinary infection and the characteristic changes which occur in the roentgenograms and in the retrograde pyelograms. The condition is not uncommonly confused with early renal tuberculosis or an infiltrating neoplasm.

The small number of cases that Alken [21] had observed did not permit him to generalize on the treatment. He stated that in his case therapy varied, but in some cases the condition is so severe that nephrectomy is necessary.

URETER

Stones.—Alyea [22] stated that the principles employed in cystoscopic removal of ureteral calculi are dilation, lubrication and anesthetization of the ureter and dislocation, grasping or crushing of the calculus.

It was suggested that complete relaxation of the ureter in its lower third is an aid in withdrawing large calculi. The most popular procedures are manipulations with catheters or bougies, spiral corkscrew stone dislodgers and cagelike instruments for grasping the calculus.

Calculi may remain in the lower third of the ureter for several years without causing serious damage to the upper portion of the tract. The calculi always have grooves in them or permit the urine to escape around them in some other way.

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21. Alken, C. E.: Die Papillennekrose, Ztschr. f. Urol. **32**:433-438 (July) 1938.

22. Alyea, E. P.: Cytoscopic Removal of Large Ureteral Calculi, Tr. Southeast. Br., Am. Urol. A., Nov. 5, 1937, pp. 11-28.

A series of 327 cases of ureteral calculi is analyzed; 72 per cent of the calculi were removed cystoscopically.

Tumor.—Hunner [23] reported a case of intussusception of the ureter in which the invagination was due to the drag of an unusually large papillomalike tumor. Microscopically, this tumor proved to be a pure polyp, thus presenting a second extremely rare, if not a unique, feature. From the history of intermittent attacks of moderate pain in the right flank for four years, Hunner concluded that the intussusception had been present for at least that length of time. There had not been vesical symptoms suggestive of involvement of the urinary tract, and the results of urinalysis on many occasions had been normal except for the presence of albumin at the time when the patient was submitted to the first investigation of the urinary tract, two years before operation. The tumor plus the intussusception had led to astonishingly little damage to the kidney, as was shown by the patient's good general health, the differential functional test and study of the removed specimen.

Hunner questioned whether the operation should not have consisted simply of excision of the tumor and reduction of the intussusception. Had biopsy tissue been taken from the tip of the tumor projecting into the bladder, the simple morphologic structure of the tumor and Hunner's knowledge of the good functional capacity of the kidney undoubtedly would have led him to save the kidney.

Foord and Ferrier [24] presented 6 proved cases and a probable seventh case of primary carcinoma of the ureter. They collected a total of 139 cases, including their own.

The basic triad of symptoms is hematuria, pain and mass. Hematuria was noted in 97, or 70 per cent, of the 139 cases; in 11 there was no bleeding, and in 31 bleeding was not mentioned. Pain is next in frequency. It occurred in 84 (60 per cent) of the cases and was absent in only 11. The tumor palpated is nearly always the hydronephrotic kidney. It is possible, however, for the kidney to be completely obstructed and not enlarged, as in Foord and Ferrier's first case. It is rarely possible to palpate a tumor of the upper part of the ureter.

On the plain roentgenogram an enlarged renal mass is often distinguishable. Stones may occasionally appear coincidentally but they seem to have little etiologic significance.

It is important that cystoscopic examination be done while bleeding is in progress, as a leading point is won by visualizing the bleeding meatus. This was observed in 26 of 81 cases in which cystoscopic exam-

23. Hunner, G. L.: Intussusception of the Ureter Due to a Large Papilloma-Like Polypus, J. Urol. **40**:752-765 (Dec.) 1938.

24. Foord, A. G., and Ferrier, P. A.: Primary Carcinoma of the Ureter, with a Report of Seven Cases, J. A. M. A. **112**:596-601 (Feb. 18) 1939.

ination was performed. Tumor tissue was observed to project in 30 of 78 cases. The projecting tumor may so obscure the meatus that it is impossible to determine whether it originates in the ureter or at the edge of the meatus. A tumor may peep through the meatus only during ureteral peristalsis, or a telltale bulge may occur at that time. With a great proportion of ureteral tumors there is a complete block and no catheter or bougie will pass beyond the tumor. This was observed in 50 cases.

Excretory urograms usually show no dye in the affected side. They may faintly outline a hydronephrosis or, rarely, show a normal kidney on the affected side. The excretory urogram is inadequate to outline satisfactorily a ureteral filling defect.

In the cases so far reported the lower end of the ureter has been by far the commonest place for the tumor to appear, 85 of the tumors having been situated in the lower third, 23 in the middle third, 20 in the upper third, 6 in the entire ureter, 2 in the middle and lower thirds and 1 in the upper and middle thirds.

All authorities agree that the treatment of choice is early surgical extirpation, which means nephrectomy and ureterectomy. For 44 nephroureterectomies in one stage the mortality was 40 per cent, whereas for 22 nephroureterectomies in two stages the mortality was 5 per cent.

In a total compiled series of 100 operations, the mortality was 34 per cent at the end of three months. Scott, in 1934, in an effort to follow collected cases in which operation was performed, could find only 2 patients alive after five years.

Transplantations.—Franche and Nguyen Trong-Hiep [25] presented the results of their experiments with implantation of the ureters into the rectum. Comparing these with the results of implantation into the bladder, they recorded as successful 25 to 30 per cent of implantations into the rectum, against 70 per cent of successes for the bladder. They accounted for the smaller number of the former by skeptic conditions in the rectal milieu, which undoubtedly plays an injurious role in cicatrization of the region of implantation. It was noted with reference to ureteropyelic peristalsis that, whereas all contemporary findings demonstrate that the ureter and pelvis respond to ascending infection with hypokinesia or akinesia, in the authors' experiments it was rather hyperkinesia that dominated in the group of failures, that is to say, the group in which implantation was followed by dilatation of the upper portion of the urinary tract.

Twenty-one experiments on dogs were reported and their results analyzed. In the first group (of 11 experiments) in which dilatation

25. Franche, O., and Nguyen Trong-Hiep: Recherches expérimentales sur l'implantation de l'uretère dans le rectum, J. d'urol. **46**:305-329 (Oct.) 1938.

occurred, two important points were established: 1. A correlation exists between ureteropyelic implantation into the rectum and an obstacle met by an exploring sound, no. 12 or no. 14. 2. This obstacle may appear as early as six or seven days after implantation. The next 4 experiments were carried out to prove whether a mechanical obstacle might exist which the exploratory sound could overcome but which offered successful resistance to the wave of urinary fluid; that is, it was thought that a kink or a torsion, alone or superimposed on a stricture, might be the cause of the dilatation. Experiments proved that this was the case. In 1 of these 4 experiments the intestine was drawn out through a laparotomy incision and sectioned at a point just opposite the site of implantation. The mouth of the ureter had assumed the appearance of a small caruncle. In spite of the continuous action of ureteral peristalsis on its contents, almost no urine entered the intestines. Such urine as did enter the intestines did so at very wide intervals through the contracted orifice of an enormously dilated ureter behind which lay a voluminous hydronephrosis (forty-two days after implantation). By compression of the lower third of the ureter between the thumb and index finger a jet of urine was forced through, which clearly revealed stenosis of the orifice. A débridement of a few millimeters of this contracted orifice was all that was needed to cause a tremendous outflow of urine into the sigmoid portion of the intestine, followed by ureteral contractions, which from that moment became effective and regular. The peritonitis that followed caused the death of the animal, so that it was impossible to carry out the intention of following the further course of this interesting experiment. But it had already revealed dramatically the importance of the mechanical obstacle and also the long conservation of the dynamism of the implanted ureter, which, far from having disappeared, had actually become exaggerated. In a final group of 6 animals the results of implantation in the sigmoid portion of the intestine, followed from seventeen days to six months, were counted successful, since there was no obstruction to the sound.

A study of these results leads to the following conclusions: 1. The dynamic ureteropyelic disturbance that sometimes follows section of the ureter is not definitive. 2. Its persistence is due, not to the traumatism itself but to its consequences, namely, stenosis of the ureter and (in 1 case) the irritative cicatricial "epine."

While most experimenters have studied the dynamism of the ureters under direct examination alone, these authors combined this with pyeloscopic examination, which, in addition to giving admirable images, has the advantage of presenting its views under almost physiologic conditions (without opening the abdomen).

BLADDER

Tumor.—Grauer [26] reported a case of leiomyoma of the bladder in a woman aged 26, who complained of intermittent attacks of frequency, urgency and difficulty of passing urine. The onset had taken place two and one-half years previously, when the patient suddenly had acute retention of urine for twenty-four hours, requiring catheterization. Attacks of frequency of urination began regularly one week after menstruation and persisted until one week before the next menstrual period. The residual urine gradually increased to 350 or 400 cc.

Cystoscopic examination revealed pronounced coarse trabeculization of the wall of the bladder with deep pockets between the muscle bundles. Arising at the internal urethral orifice and extending intravesically so as to involve the left and anterior portion of the internal urethral orifice was a smooth, round lobe of firm tissue about 4 cm. in diameter, so situated that it obstructed the outflow of urine. The appearance "was not unlike that of a large left lateral lobe, prostatic hypertrophy." It was covered with normal vesical mucosa.

A suprapubic cystotomy and resection of the tumor was done.

The diagnosis was submucous leiomyoma of the neck of the urinary bladder.

Barringer [27] stated that three-year cures by radium in 215 cases of cancer of the bladder at Memorial Hospital occurred in 69 cases (32 per cent). Five year cures occurred in 52 cases (24.1 per cent), a drop of 7.6 per cent. The total number of cases in which the bladder became "cancer-free" was 96 (44.6 per cent).

The cancers in the cases were treated cystoscopically and by suprapubic implantation.

The authors included all cases, no matter how extensive the involvement, in which the bladder was opened. Radium was implanted in many extensive carcinomas "with the idea of controlling more cancers." Notwithstanding this effort, attempts to produce five year cures failed in about three fourths of all cases.

It is noteworthy that tumors of grade 4 have been controlled in only 2 cases. Barringer believed that with proper methods of irradiation carcinoma of grade 4 should not be more difficult to control than carcinoma of any other grade.

In most cases of fatal carcinoma death occurs within the first year. The chief cause of death is unquestionably severe infection of the bladder and kidneys. Probably few patients actually die of carcinoma.

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26. Grauer, T. P.: Leiomyoma of the Bladder, J. Urol. **40**:594-597 (Nov.) 1938.

27. Barringer, B. S.: Radium-Therapy of Bladder Carcinoma: Five-Year Results; Failures; Future Therapy, J. Urol. **40**:606-611 (Nov.) 1938.

The Carcinoma Registry has emphasized that vesical cancers are more often multiple than single. They have even seen fit to change the pathologic diagnosis from papilloma to carcinoma on the clinical basis that carcinomas are multiple. From the clinical standpoint, the fact that there are several tumors instead of one indicates in a broader sense that multiplicity of tumors constitutes a malignant element as compared with solitary tumors. On the other hand, from Barringer's records, carcinomas of the bladder are usually single.

The implantation of seeds into an infected tumor increases the severity of infection. A slough is always formed, and this presents a focus of increased infection. This slough may become incrusted with calcareous deposits, and the formation of stone results. Asepsis and a certain amount of antisepsis help to obviate this condition.

Vesicovaginal fistulas may occur as the result of implantation of radon or the depth of the tumor or both. Barringer has observed 3 cases in which such fistulas were present.

Not only the size of the tumor but the infection of the tumor and the condition of the kidneys should determine whether suprapubic or cystoscopic treatment is to be used. Barringer stated that he leans more and more toward cystoscopic treatment. If the tumor is ulcerated and infected and if one or both of the kidneys are hydronephrotic, the suprapubic implantation of a large amount of radon is a dangerous procedure from the standpoint of the infection.

Incontinence.—Gomez B [28] stated that during parturition the prolonged compression of the vesical neck and the urethra between the bony planes of the fetal head on the one hand and the os pubis on the other not infrequently results in injury to the sphincter of the vesical neck, which under certain conditions produces incontinence. This may develop gradually during years, or it may appear promptly after a brief period of retention owing to inflammation of the vesical neck and the urethra accompanied by paralysis of the bladder. Such retention may be total or partial. Distention, residual urine and cystocele formation act progressively on the sphincter, stretching its fibers until it finally becomes insufficient. In some cases insufficiency may result from the simple wounding of the sphincter, without the presence of other complications. In any case, the incontinence tends to be progressive, until finally the loss of urine is constant whenever the patient assumes the upright position.

Treatment is surgical. Of the many procedures that have been tried, the best is that of Marion. With the patient in the gynecologic position, a Pezzer catheter is introduced into the urethra in such a way that its

28. Gomez B, Carlos: Incontinence d'urine chez la femme par relachement du sphincter vesical et son traitement, J. d'urol. **46**:344-356 (Oct.) 1938.

tip rests against the vesical neck, where it serves as a landmark at the moment of dissection. After suitable retraction of the vaginal walls and the labia minora, a transverse incision is made in the vaginal mucosa, 3 to 4 cm. long, passing 2 or 3 mm. behind the meatus. The mucosa is grasped with a forceps and its dissection continued bluntly with a compress of gauze or with blunt-pointed scissors over an extent not less than 5 cm. until the entire region of the neck is uncovered. In dissection of the vaginal flap, the largest possible amount of muscular and fibrous tissue should be left to insure greater solidity.

Reconstruction of the vesical neck and the urethra is then begun, nonabsorbable sutures of linen or silk being used. With a Jalaguier needle a U suture is passed transversely in front of the urethra through the deepest part of the musculofibrous tissues which lie on each side of the midline. This is followed by two or three more sutures of the same kind, placed below the first in such a way that when they are tied they draw with them, under the vesical neck and the urethra, the lateral muscular and fibrous tissues. Emphasis is laid on the great care with which the first of these deep sutures must be placed, since if it perforates the vesical mucosa a vesicovaginal fistula is likely to result.

This done, the levator muscles on both sides are looked for and sutured in a second plane, transversely, with linen threads, as in an anterior colporrhaphy. Last of all, the vaginal mucosa is sutured at right angles to the other sutures, which it covers; this may be done with horsehair, agraffes or linen. With a tampon of iodoform gauze in the vagina, the operation is finished. This dressing is not removed until the fifth or sixth day, the patient being kept in complete immobility and in a state of constipation. Sutures are removed after nine or ten days. During all this time the catheter remains in the urethra, and care must be taken that it does not become clogged. After its removal on the twelfth day, the patient may not be able to urinate spontaneously for another week. In such cases (and these are among the best) catheterization should be done with a very small catheter. Eight cases are reported briefly.

Miller [29] stated that cystograms taken with the patient in the anteroposterior and oblique views in the dorsal, erect and erect straining positions yield information valuable in the selection of an operative procedure for repair of cystocele in individual cases. They are useful also in evaluation of the repair.

Urethrograms have proved an aid to investigation of the causes of incontinence and residual urine and have indicated the need, during repair, for special attention to narrowing the vesical neck and urethra,

29. Miller, J. D.: Studies on Cystocele and Urinary Incontinence in the Female by Use of Cystograms and Urethrograms, J. Urol. **40**:612-623 (Nov.) 1938.

correcting injuries to the trigonalis muscle and/or providing adequate fixation at the level of the internal sphincter.

Day and Martin [30] stated that in practically every case of vesical diverticulum there is evidence of increased intravesical pressure over a long period, almost always caused by obstruction at the outlet of the bladder.

Of their 69 patients, 42 had contracture of the vesical neck, 25 had benign hypertrophy, 1 had congenital valves in the posterior portion of the urethra and 1 had a filiform stricture in the urethra.

In approximately 75 per cent of cases the orifice is situated from 1 to 3 cm. above the interureteral ridge, either mesial or lateral to the ureteral meatus.

The sacs vary from pouches the size of a hazelnut to giant diverticula with a capacity of 2 liters or more. Small diverticula are of little importance if the obstructing lesion is overcome; otherwise they grow, although slowly.

In contradistinction to the site of the orifice, the direction of the protrusion varies. The sacs may extend between the rectum and the bladder nearly as far as the subpubic ligament and in addition well up on the superior surface of the bladder.

The first and fundamental consideration is surgical relief of the obstruction. After this has been accomplished, the diverticulum will seldom increase in size. If the sac is not large, empties fairly well and is not badly infected, diverticulectomy is unnecessary in many instances. On the other hand, if the diverticulum is of the retention type or is large, excision is indicated, provided that the patient is a fair surgical risk.

In many cases an operation in three stages is advisable; that is, preliminary cystostomy drainage should be performed with or without drainage of the diverticulum itself by means of an accessory Pezzer catheter introduced through the wall of the diverticulum. In due course this should be followed by diverticulectomy and finally by surgical attack on the obstruction.

Day and Martin [30] studied 69 cases of vesical diverticulosis in twenty-five years. In 51, operation was performed for relief of obstruction at the vesical neck, and in 32 diverticulectomy was performed. Of the latter, prostatectomy was done in 17, resecting of the vesical neck in 14 and electrodestruction of congenital valves in 10. There were 3 deaths, and in 3 other cases the results were poor. In 1 of these cases the ureter opened into the diverticulum, and in another case four diverticula were excised, leaving a small contracted bladder.

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30. Day, R. V., and Martin, H. W.: Vesical Diverticulum, J. A. M. A. **112:** 509-513 (Feb. 11) 1939.

Bilharziasis.—Campbell [31] stated that vesical bilharziasis is not common in the United States but is found chiefly in the Mediterranean countries and is endemic in Egypt, Greece, Syria, Uganda, Turkey and South Africa. The antihelminthic hospitals of Egypt alone treat the condition in over a quarter of a million cases a year. In the United States about 30 cases have been reported.

Three trematodes of the genus Schistosomum which infest the human body are first, Schistosomum mansoni; second, Schistosomum japonicum and last Schistosomum haematobium, which is of chief interest to the urologist because the outstanding lesions caused by its presence are in the urinary tract. These parasites are found especially in Africa, India, Mesopotamia, Madagascar, Greece and Japan. Their ova, unlike those of both the previously mentioned species, have terminal spines and may be found both in the urine and in pathologic tissues.

Although the urinary tract, especially the bladder, is the most common site of the lesions, Schistosomum haematobium may also affect the epididymis, prostate gland, seminal vesicles, corpora cavernosa, corpus spongiosum, urethra and female genitalia.

The parts of the bladder most commonly involved by bilharzial lesions are the trigon, the ureteral orifices and the posterior wall. The summit of the bladder is usually the last site to be involved but in cases of advanced involvement may be the place where characteristic lesions are seen.

There may be few symptoms of the disease; after penetration of the cercariae, headache, malaise, fever and cough may occur, together with pruritus and erythema at the point of entrance. The urinary symptoms may occur from three or four weeks to several years after inoculation. Hematuria, the most constant symptom, is often the only one. It is usually terminal, and it may not occur if only deep-seated lesions are present. If secondary infection is present, irritability of the vesical neck will be present, and often there are suprapubic pain, chills and fever. A rather marked anemia with a low color index is often associated with the picture. There may be slight leukocytosis and eosinophilia.

Diagnosis in sections of the world where the disease is common is not difficult, but in parts where the condition is unusual the diagnosis may be dependent on competent pathologic examination of specimens at biopsy, in which ova are usually seen embedded in the tissues. Other methods of diagnosis are examination of the urine for ova, cystoscopic examination and roentgen examination. The ova are ovoid, about 140 microns in length and narrowed at one end, to which is attached a terminal spine. Cystoscopic examination reveals the rather typical lesions

31. Campbell, D. A.: Vesical Bilharziasis: A Case Report, J. Urol. **40**:598-605 (Nov.) 1938.

previously described. Roentgen examination may show a dense homogeneous cloudlike shadow limited to vesical contour or to one or another part of the ureter, and to the general thickening of the walls of the affected part on account of the presence of calcified eggs irregularly deposited but not in sufficient numbers or concentration to throw a dense calcareous shadow of the organ. Definite calcified demarcations are pathognomonic, but cloudy shadows are only highly suggestive, as chronic cystitis from other causes may produce them.

Emetine hydrochloride papaverine, emetine periodide, antimony sodium thioglycolate, antimony thioglycollamide and carbon tetrachloride have all been used successfully. Christopherson found that the use of antimony and potassium tartrate killed the parasite and destroyed the viability of the ova. At that time he recommended the use of doses of 2¼ grains (0.14 Gm.) each until 20 to 30 grains (1.3 to 2 Gm.) had been used. Later a new compound, called fuadin, was found to cure bilharzia disease in the majority of cases. Campbell stated that Khalil and Betache recommended intramuscular or intravenous administration of 1.5 cc. on the first day, 3.5 cc. on the second, 5 cc. on the third and 5 cc. every other day until a total of ten injections, or approximately 40 cc., had been given. Basing their conclusions on 1,474 cases, these investigators found the reactions to be practically negligible, and only 4 per cent of the patients were not cured after completion of the course of treatment. In this group of 4 per cent an additional course of three injections was found to be sufficient.

Campbell reported a case of this condition in a 21 year old patient who was treated with fuadin.

(To Be Concluded)

News and Comment

Biological Photographic Association.—The ninth annual convention of the Biological Photographic Association will be held September 14 to 16 at the Mellon Institute for Industrial Research, Pittsburgh. The program will be of interest to scientific photographers, scientists who use photography as an aid in their work, teachers in the biologic fields, technical experts and serious amateurs. It will include discussions of motion picture and still photography, photomicrography, color and monochrome films and processing, all in the field of scientific illustrating. Up-to-date equipment will be shown in the technical exhibit, and the print salon will display the work of many of the leading biologic photographers in the United States and abroad.

The *Biological Photographic Association Journal* is published quarterly and constitutes a volume of about 250 pages, which is furnished free to members. Membership privileges include an authoritative question and answer service and the right to borrow loan albums and exhibits of scientific prints for study and display.

Further information about the association and the convention may be obtained by writing the secretary of the Biological Photographic Association, University Office, Elizabeth Steel Magee Hospital, Pittsburgh.